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ANTIBODY FORMATION IN EARLY INFANCY AGAINST DIPHTHERIA AND TETANUS TOXOIDS

JEAN V. COOKE, M.D., WITH THE ASSISTANCE OF JEAN HOLOWACH, M.D., J. E. ATKINS, JR., M.D., AND JOHN R. POWERS, M.D.

ST. LOUIS, MO.

THE belief that there is a striking defect in the ability of young infants to produce specific antibodies has been rather widely held and has been the basis for the practice of deferring active immunization until later infancy. The present paper is the report of a study made on a group of infants to determine their ability to produce specific antibodies against two antigens, diphtheria and tetanus, antitoxins of which can be more or less accurately determined quantitatively and are generally accepted to be associated with clinical immunity.

METHOD OF STUDY

The infants tested were healthy babies in attendance at the Health Centers at Washington University Pediatric Clinic and at one of the St. Louis City Health Clinics and included both white and Negro children. Their ages varied from 1 to 14 months, although most subjects were under 6 months of age. At the first visit, blood was drawn, tested for diphtheria and tetanus antitoxins, and a subcutaneous injection of combined diphtheria and tetanus toxoid* given. A second injection of the same material was given two months later, and one month after this second injection a blood sample was again titered for diphtheria and tetanus antitoxin. No unusual local or general reactions followed the injections. Schick tests were performed on all babies after the immunization, but so few of the children returned for the readings that no analysis of the results could be made.

RESULTS

Tetanus.—In a total of 284 infants from 1 to 14 months of age tested before immunization, none had detectable tetanus antitoxin in the blood. All had

From the Department of Pediatrics, Washington University, and the Washington University Clinics.

*The toxoid antigen used was combined Diphtheria-Tetanus Toxoids Alhydrox (Cutter), and the dose given was one cubic centimeter. The material was furnished by the Cutter Laboratories, and all antitoxin titrations using the standard guinea pig method were done by the Cutter Laboratories, Berkeley, Calif., under the direction of Mr. R. B. Clark, Supervisor of Clinical Research.

less than 0.01 unit per cubic centimeter, the smallest amount detectable by the method used. The results of tests one month after the second injection of toxoid in 188 infants are shown in Table I. It will be noted that 181 showed one unit or more of antitoxin per cubic centimeter. Five of the 127 in whom the immunization was started before the age of 6 months showed between 0.3 and 1.0 unit, while only two babies, both over 6 months of age, showed as little as 0.01 to 0.1 unit of antitoxin.

TABLE I. RESULTS OF IMMUNIZATION WITH TETANUS TOXOID IN 188 INFANTS

AGE AT FIRST TOXOID INJECTION (MO.)	NUMBER IMMUNIZED	ANTITOXIN TITER AFTER IMMUNIZATION, UNITS PER CUBIC CENTIMETER		
		0.01 TO 0.1	0.3 TO 1	1 OR MORE
1 to 3	73		4	69
3 to 6	54			53
6 to 14	61	2	1	59
Total	188	2	5	181

These results show that the mechanism for producing antibodies, as judged by the response to tetanus antigens, is well developed even in early infancy, since more than 95 per cent of those first inoculated from 1 to 6 months of age developed an excellent immunity, and in the remainder the antibody response was very good. Indeed in only two, or a little more than one per cent of 188 infants immunized, could the response be considered inadequate.

TABLE II. DIPHTHERIA ANTITOXIN FOUND IN 284 NORMAL INFANTS

AGE (MO.)	NUMBER TESTED	DIPHTHERIA ANTITOXIN TITER, UNITS PER CUBIC CENTIMETER			
		LESS THAN 0.03	0.03 TO 0.1	0.1 TO 1.0	1.0 OR MORE
1 to 3	112	75 (67 %)	9	18	10
3 to 6	90	74 (82.2%)	8	6	2
6 to 14	82	79 (96.3%)	0	2	1
Total		228 (80.3%)			

Diphtheria.—Of 284 infants from 1 to 14 months old tested for diphtheria antitoxin before immunization, 228, or 80 per cent, had less than 0.03 unit of antitoxin per cubic centimeter. However, as was to be expected, the proportion of those with demonstrable passive immunity varied considerably with the age of the baby, as shown in Table II. Here it will be noted that of those under 3 months of age, about one-third had antitoxin, while of those from 3 to 6 months old less than one-fifth had a passive immunity, and in the babies over 6 months less than 4 per cent had antitoxin. The number of infants in the early months of life who had a passive diphtheria immunity inherited from their mothers was somewhat less than in studies reported previously, and the possible reasons for this will be discussed later.

After immunization, 191 of the infants were tested. A summary of the results is shown in Table III. Those who showed more than 0.1 unit of antitoxin per cubic centimeter were considered to have developed a definite immunity. It will be noted that in the group of seventy-five infants under 3 months of age, one-third failed to reach a titer of 0.1 unit or more while of those

TABLE III. RESULTS OF DIPHTHERIA IMMUNIZATION IN 191 INFANTS

AGE (MO.)	NUMBER TESTED	ANTITOXIN TITER AFTER IMMUNIZATION, UNITS PER CUBIC CENTIMETER				
		LESS THAN 0.03	0.03 TO 0.1	0.1 TO 1.0	1.0 OR MORE	PER CENT WITH 0.1 UNIT OR MORE
1 to 3	75	17	8	17	33	66.6
3 to 6	56	4	2	12	38	89.3
6 to 14	60	1	2	13	44	95.0
Total	191	22	12	42	115	82.2

from 3 to 6 months almost 90 per cent, and of those over 6 months, 95 per cent had developed immunity.

The relation of the presence of passive antitoxin in the blood and resistance to immunization in younger infants in this group was analyzed. In Table IV are shown the results of immunization of 158 infants who showed less than 0.03 unit of antitoxin before the toxoid injections. It will be seen that even in the younger infants under 3 months of age, 83 per cent developed immunity, although the figures of 87 per cent in those 3 to 6 months old and 95 per cent in the age group over 6 months are definitely better.

TABLE IV. DIPHTHERIA IMMUNIZATION IN 158 INFANTS WITH NO PASSIVE IMMUNITY

AGE (MO.)	NUMBER TESTED	ANTITOXIN TITER AFTER IMMUNIZATION, UNITS PER CUBIC CENTIMETER				
		LESS THAN 0.03	0.03 to 0.1	0.1 TO 1.0	1.0 OR MORE	PER CENT WITH 0.1 OR MORE
1 to 3	52	7	2	12	31	82.7
3 to 6	46	4	1	7	34	87.0
6 to 14	60	1	2	13	44	95.0

The results of immunization of thirty-three babies in whom antitoxin was present before immunization are shown in Table V. When attempting to determine the development of an active antitoxic immunity in a group of infants who already have a passive antitoxic immunity, the interpretation of the results depends upon whether or not the titer has risen after the immunization. In most of the infants studied the antitoxin titer was lower after the toxoid injections than before. The striking defect in active antitoxin formation is shown by the fact that less than one-third of the infants under 3 months of age had more than 0.1 unit of antitoxin per cubic centimeter, whereas almost 83 per cent had had such a titer before immunization. In a review of the individual infants no constant quantitative relationship was found between the amount of passive antitoxin present and the inability to develop an active immunity,

TABLE V. DIPHTHERIA IMMUNIZATION IN 33 INFANTS WITH PASSIVE IMMUNITY

AGE (MO.)	NUMBER TESTED	DIPHTHERIA ANTITOXIN TITER IN UNITS PER CUBIC CENTIMETER							
		BEFORE IMMUNIZATION			AFTER IMMUNIZATION				
		0.03 TO 0.1	0.1 TO 1.0	1.0 OR MORE	LESS THAN 0.03	0.03 TO 0.1	0.1 TO 1.0	1.0 OR MORE	PER CENT WITH 0.1 OR MORE
1 to 3	23	4	11	8	10	6	5*	2	30.4
3 to 6	10	4	4	2	0	1	5†	4	90.0

*Three of these were the same, and one was less than before immunization.
†Two of these were the same, and one was less than before immunization.

since some infants with the lowest titer (0.03 to 0.1 unit) had less than 0.03 unit when retested after immunization. While the result appeared better in the small group of infants 3 to 6 months old, it was true that in some of these in whom the antitoxin content appeared good, the titer was the same or slightly less after than before the toxoid was given, as was the case in the younger age group. Although the number of passively immune babies studied is relatively small, the results are so definite and striking as to leave little doubt as to their significance.

To summarize briefly, it was found that so far as tetanus antigen is concerned, the mechanism for the production of specific antibody (antitoxin) is apparently as good in early infancy as it is later, since practically all infants showed an excellent response. With diphtheria antigen, infants under 3 months of age responded to active immunization poorly, and this interference with antibody production was due to the presence of recognizable passive immunity in most instances. Even small amounts of demonstrable antitoxin may prevent the active immunity, and it seems possible that this fact may explain the decreased percentage of subjects in the 3-to-6-month age group who developed immunity. After the age of 6 months, good immunity developed in 95 per cent.

DISCUSSION

The long-held belief that young infants respond poorly to antigens has been accepted by most authorities and has been the reason for the general practice of deferring active immunization until the latter half of the first year. This has been supported by some observations in rabbits that young animals produce antibodies less well than older ones, and by the fact that many infections are more severe and fatal in the neonatal period and in the early months of life than later, although it has long been realized that immunity to vaccinia develops as readily in early infancy as later. The principal reason, however, is apparently derived from the views of Dr. William H. Park and his co-workers in their pioneer work with active immunization in children against diphtheria, which really formed the basis and pattern for much of the subsequent development of active immunization. The statement is made frequently in their papers that immunization should be deferred until after 6 months, and this conclusion was apparently reached from the following observation,[1] which is the only direct reference to the subject in their many reports:

> "Two thousand infants were given full doses of toxin-antitoxin on the third, eighth, and eleventh days after birth. One year later 100 were tested, and 52 per cent gave negative Schick tests. Since untreated infants gave the same result, it was evident that the combined effect of the immature cells and the over-neutralization of the toxin-antitoxin present (because of the passive immunization derived from the mother) prevents any appreciable response to the toxin-antitoxin injections."

In diphtheria it has been generally accepted that passive immunity in early infancy as indicated by a negative Schick test interfered with active immunization, although the present paper reports the first time this has been demonstrated

by actual antitoxin determinations. This inhibition of active antigen stimulus by passive immunity is apparently identical with that which has been shown in artificial passive tetanus immunity,[2] and is apparently due to the fact that toxoid antigen combines with antitoxin, and the neutralized antigen cannot exert the usual antigenic stimulus.

The number of infants in the series here reported who had a passive immunity in the early months of life was only about 34 per cent, a figure which is less than half of that reported by Karasawa and Schick and by v. Gröer and Kassowitz in studies of more than thirty years ago. Because of these early reports the belief is still widely held that a considerable majority of young infants possess a high degree of immunity to diphtheria for some months after birth. It should be remembered, however, that in the days when most of such studies were made (1915-1922) diphtheria was relatively prevalent in the large cities from which statistics were collected, and the percentage of 65 to 72 per cent of natural immunes is no longer applicable to most populations. Even then the figures[3] from rural and suburban districts where diphtheria was less common showed only 42 to 48 per cent of immunes. In recent times, Wright and Clark,[4] in a study of 250 parturient women from suburban London, found 44 per cent had negative Schick tests, while Vogelsang and Kryvi[5] in Bergen, Norway, found only 27 per cent of 500 such women to have negative Schick tests. It is apparent, therefore, that there is no justification for applying generally the results of the early surveys to modern populations, in whom the percentage of immunes is often less than in a previous generation because of differences in the incidence of the disease.

The possibility has been suggested that in the United States, where active diphtheria immunization is practiced on many children, a definite increase in antitoxin immunity might have developed and persisted to adult life. On the other hand, in the past decade the incidence of diphtheria has fallen, so that in the United States the mortality from the disease is now less than 5 per cent of what it was when most of the studies were made; thus it would be expected that the number of natural immunes would be considerably lower. This seems to be substantiated by the fact that in a group of 2,933 troops of the United States Army from widely scattered areas of the United States, 55 per cent had negative Schick tests.[6] It must be concluded that from one-third to one-half of infants have a passive diphtheria immunity in the early months of life. This immunity persists in various infants up to 6 months, and while it is present, the infants are resistant to active immunization with diphtheria antigens. It would appear advisable, therefore, to defer active diphtheria immunization until after the sixth month since at this time the highest percentage of active immunes would be obtained.

The chief interest in immunizability of young infants and their immunity response mechanism, and the main reason for the present study, concerns the use of whooping cough antigens. Diphtheria and tetanus are at present such a slight hazard in early infancy that there appears no valid necessity for attempting early immunization. The well-known mortality of pertussis during the first year of life, however, has stimulated interest in the possibility of

immunization in the early months since no one questions the desirability of early active immunization against whoopng cough if this is possble. The belief in the poor response to antigens by young infants has been so strong that it is the routine practice to give pertussis immunization only after the sixth month, although a few physicians have been attempting earlier injections. In a recent well-controlled field study, Sako[7] has reported that he found early pertussis immunization as effective as that done in later infancy. The evidence presented in the present study shows conclusively that the mechanism for antibody formation against tetanus antigen is as well developed in early infancy as it is for vaccinia, and that only when a passive antibody is present as in certain cases of inherited diphtheria immunity is there an interference with antibody formation. If the ability to produce specific antibodies is well developed in early infancy, there appears no reason that antibodies to pertussis antigen cannot be as readily formed as those to tetanus antigen, and the justification for early pertussis immunization is strengthened.

Recently, there has been some tendency to use a routine of diphtheria, pertussis, and tetanus antigens by simultaneous injection. While such multiple antigens are as effective in immunization as those given individually, they would seem to be most useful when given to infants after 6 months of age. Since, for the reasons stated, there are definite advantages in immunizing against diphtheria later in infancy and against pertussis in the early months, the "timing" is bad for routine use of combined antigens. A course which appears to meet the requirements as discussed, and which has been in use in the Washington University Children's Clinic for the past year, is to give pertussis vaccine at the sixth, ninth, and twelfth weeks, and combined diphtheria and tetanus toxoids in the seventh and ninth months.

SUMMARY

A study was made of the development of antitoxin after two injections of combined diphtheria and tetanus toxoids in a group of young infants. It was found that the production of tetanus antitoxin is as good in the early months of life as later, and this finding denotes that the mechanism for the production of antibodies is well developed in young infants. With diphtheria antigen, the development of antitoxin is definitely defective in a considerable number during the first 6 months of life. This impairment of antibody formation is related to the presence of passive immunity in the resistant infants and appears specific for diphtheria. The application of these findings to the practical immunization of infants to diphtheria, tetanus, and whooping cough was discussed.

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GALACTOSEMIA

EUGENE O. GOLDSTEIN, M.D., AND JULIUS M. ENNIS, M.D.
BALTIMORE, MD.

GALACTOSEMIA, chronic hypergalactosemia, galactemia, and galactose diabetes are terms used to designate a metabolic disorder of infancy, characterized by the symptoms of failure to gain weight and grow properly, with the chief signs of hepatomegaly, splenomegaly, melituria, and albuminuria.

The first authentic case was reported by Göppert[1] in Germany in 1917. His patient was 2 years and 5 months of age when first observed. The child had had a history of jaundice for the first eight months of life, was poorly developed, malnourished, had a large liver, and there were albumin and sugar in the urine. The reducing substance was found to be galactose, and when milk was removed from the diet, sugar and albumin disappeared from the urine, the child gained weight, and the liver became smaller.

In 1935, Mason and Turner[2] published the first American report of a case in a Negro boy 6 months old who failed to gain normally as long as his diet contained milk, who showed marked enlargement of the liver and slight enlargement of the spleen and superficial lymph nodes, a positive van den Bergh, secondary anemia, osteoporosis, and albumin and sugar in the urine. The sugar was determined to be galactose. Removal of milk from the diet resulted in the disappearance of sugar and albumin from the urine, decrease in the size of the liver and spleen, improvement in the anemia and the osteoporosis, and disappearance of the positive van den Bergh with a rapid gain in weight.

Norman and Fashena[3] in 1943 published the third case, in an 11-week-old white child, characterized by galactosuria, albuminuria, hepatosplenomegaly, mild azotemia, and osteoporosis. Removal of milk from the diet resulted in disappearance of all symptoms except the mild azotemia.

Mellinkoff and his associates[4] in 1945 reported a similar patient, first seen at the age of 2 months, who in addition had evidence of liver damage as shown by a positive cephalin flocculation test. He also improved on a milk-free diet and had gained weight and appeared normal except for an enlarged liver at 7 months of age.

Bruck and Rapoport[5] in the same year reported another case similar in all respects to the previous cases, in which there were, in addition, bilateral nuclear cataracts. All pathologic signs and symptoms including the cataracts disappeared when milk was removed from the diet. They also reported that cataracts were later discovered in Mason and Turner's patient.

The most recent article on galactosemia by Goldbloom and Brickman[6] in July, 1946, reports two patients, aged 6 and 2½ months, with similar findings

From the Department of Pediatrics, Sinai Hospital, Baltimore, Md. Dr. A. J. Schaffer, Chief of Service.

including cataracts, who improved satisfactorily upon elimination of milk from the diet. The cataracts alone failed to clear.

There are several cases reported in the older literature in which galactose has been found in the urine, but because of other coexisting conditions they cannot be placed in the category of galactosemia.

We will report another case, bringing the total of the published cases to eight.

CASE REPORT

W. J., a white male infant, was admitted to the Children's Ward of the Sinai Hospital of Baltimore on May 28, 1947, at the age of 2½ months, with a chief complaint of vomiting and diarrhea since birth.

Family History.—The parents were both 35 years old and in good health. There were two siblings, aged 18 and 20 years, both living and well. The mother had had one abortion in the first trimester, cause unknown. A maternal grandmother was a known diabetic.

Past History.—The child was born at term and delivery was uneventful. The birth weight was 8 pounds. He became jaundiced on the third day of life and remained so for one week.

Present Illness.—From the age of 2 weeks the child began to vomit his feedings, requiring frequent changes of formula.

At one month of age he developed coryza with cough, and at that time he developed a diarrhea lasting two days. He was treated with one injection of penicillin. Following this he had a constant cough, sneezing, and associated sweating and pallor. There were alternating vomiting, diarrhea, and constipation. One week prior to admission his stools became greenish in color and mucus was noted on several occasions. The mother had noticed frequent swallowing of air, with eructation and flatulence. The child was noted to ruminate after regurgitation of food. He always seemed hungry, and he lost weight. He was seen by Dr. Askin on the day of admission, who found an enlarged liver and recommended hospitalization for investigation with a working diagnosis of von Gierke's disease.

Physical Examination.—The temperature was 100° F., pulse 140, respiration 26, weight 7 pounds, 8½ ounces, head 38 cm., chest 30½ cm., length 59 cm. Examination revealed a small, poorly nourished, pale, 2½-month-old white male infant, who appeared acutely ill. He was alert and his cry was vigorous. Bilateral zonular cataracts were observed. The abdomen was protuberant. The liver was smooth, enlarged, and firm, the edge reaching three fingers below the costal margin. Laboratory findings were as follows: STS and tuberculin tests were negative; the red blood count was 3.11 million, hemoglobin 8.0 Gm., white blood count 25,300, with 58 per cent polymorphonuclear cells. The original urine showed a 2 to 3 plus albumin; it was negative for sugar and acetone. Several morning urine specimens revealed no sugar, but on the fourth day a specimen taken a short time after feeding revealed a one plus sugar. Thereafter, repeated urinalyses revealed varying amounts of sugar from a trace to 4 plus by the qualitative Benedict's test, and albumin from a trace to 2 plus by the heat and acetic acid test. The fasting blood sugar (venous blood) was 79 mg. per cent, cholesterol 192 mg. per cent, calcium 11 mg. per cent, total protein 5.5 Gm. per cent, albumin-globulin ratio 3.8/1.5. The bilirubin was 7.0 mg. per cent. The direct van den Bergh was 1.1 mg. per cent. The thymol turbidity was 4.7 units; the alkaline phosphatase was 8.4 units; the bromsulfalein revealed no retention in thirty minutes. The PSP test showed 90 per cent excretion in three hours. The prothrombin time was thirty-seven seconds, with a control of thirty seconds. The x-ray of the chest was negative. A roentgen examination of the abdomen revealed "intestine displaced to the left and downward by a mass, probably an enlarged liver; the long bones were not remarkable." The presence of a reducing substance and albumin in the urine, associated with retardation in growth and development, cataracts, and an enlarged liver, suggested the condition of galactosemia.

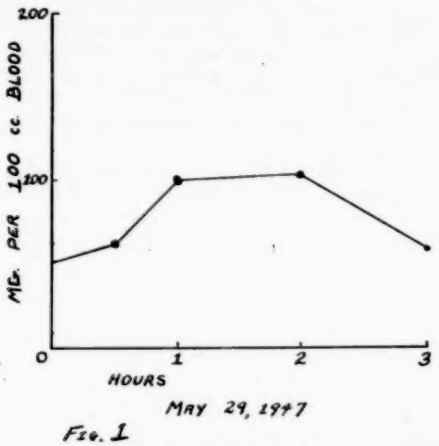

Fig. 1.—Total blood sugar values after the ingestion of 1.75 Gm. of glucose per kilogram of body weight.

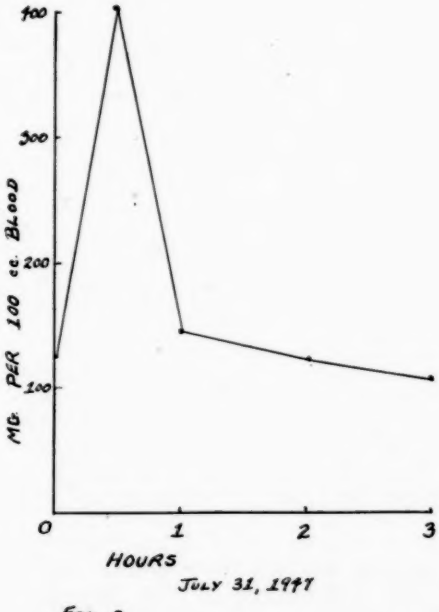

Fig. 2.—Total blood sugar values after the ingestion of 1.75 Gm. of galactose per kilogram of body weight.

Identification of the sugar in the urine was then undertaken.* Fermentation with baker's yeast was shown to be negative. Osazone crystals were prepared, which could not be distinguished from galactosazone. Mucic acid crystals were obtained, identical with those obtained with galactose. The phloroglucinol test was reported as equivocal. The reducing substance in the urine was thereby identified as galactose. A glucose tolerance test was done and a normal curve obtained. An oral galactose tolerance curve was also done. The blood sugar rose to 400 mg. per cent one-half hour after the ingestion of 1.75 Gm. of galactose per kilogram. (See Figs. 1 and 2.)

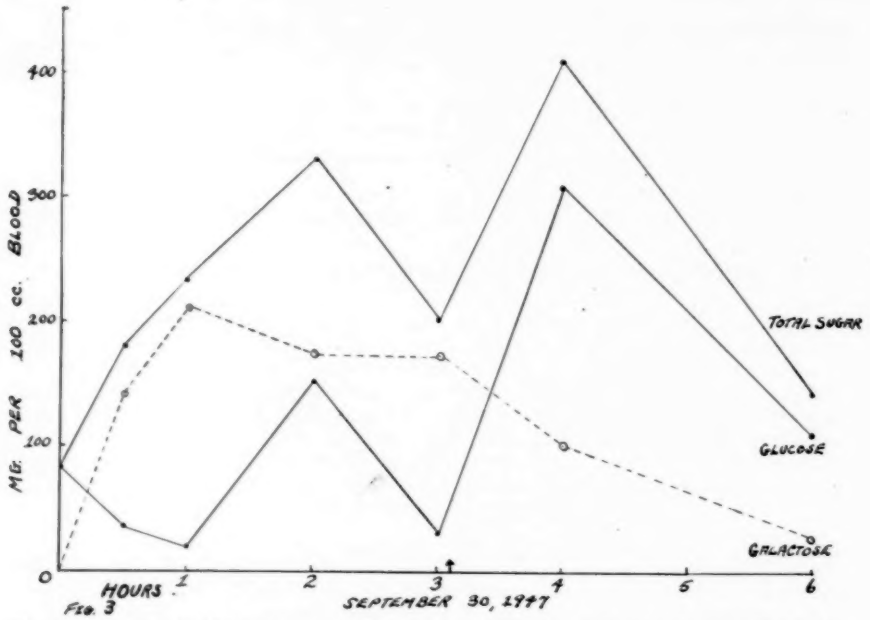

Fig. 3.—Values for total blood sugar, glucose, and galactose after the ingestion of 1.75 Gm. of galactose per kilogram of body weight.

Course in Hospital.—On the basis of identification of urinary sugar as galactose and an abnormal galactose tolerance curve, a diagnosis of galactosemia was made and the child put on a milk-free diet. A Nutramigen and cane sugar formula was substituted for milk. On this regime the urine became free of albumin and the reducing substance. The child began to gain weight, increasing from 7 pounds, 8½ ounces on admission to 9 pounds, 10½ ounces on discharge nine and one-half weeks later. The liver was somewhat smaller at the time of discharge, and the vomiting had ceased. The child was discharged to return later for further study.

He was readmitted on Sept. 28, 1947, at the age of 6½ months, seven weeks after discharge, during which time he had gained three pounds, 7 ounces. Physical examination revealed a well-nourished, fairly well-developed white male child, alert and active. The cataracts had completely disappeared. The abdomen was full, and the liver edge was palpable 3 fingerbreadths below the costal margin. Laboratory studies revealed the following: The red blood count was 3.4 million, the hemoglobin 8.4 Gm., the white blood count was

*We are indebted to Dr. Harold Harrison of Baltimore City Hospitals for aid in identification of the urinary sugar.

11,100 with 27 per cent polymorphonuclear cells and 73 per cent lymphocytes. The urine was negative for albumin, sugar, and formed elements. The urea was 16 mg. per cent, the fasting blood sugar 68 mg. per cent. The total proteins were 6 Gm. per cent, the albumin-globulin ratio was 4.5/1.5, and the van den Bergh was negative. The cholesterol was 148 mg. per cent, with 58 per cent esters. The calcium was 11.4 mg. per cent and the phosphorus, 4.5 mg. per cent. The carbon dioxide combining power was 41.2 volumes per cent. A glucose tolerance test was done. After the ingestion of 1.75 Gm. of glucose per kilogram, a normal or slightly flattened curve was obtained. A galactose tolerance curve after the ingestion of 1.75 Gm. of galactose per kilogram showed a high rise in one hour and a reduction to almost fasting level in six hours. Depression of the glucose level coincident with the rise of blood galactose was shown. During this test, 7.81 Gm. of galactose was excreted in the urine. On one occasion the glucose (blood) fell to 19 and on another to 8, without evidence of shock. (See Figs. 3 and 4.)

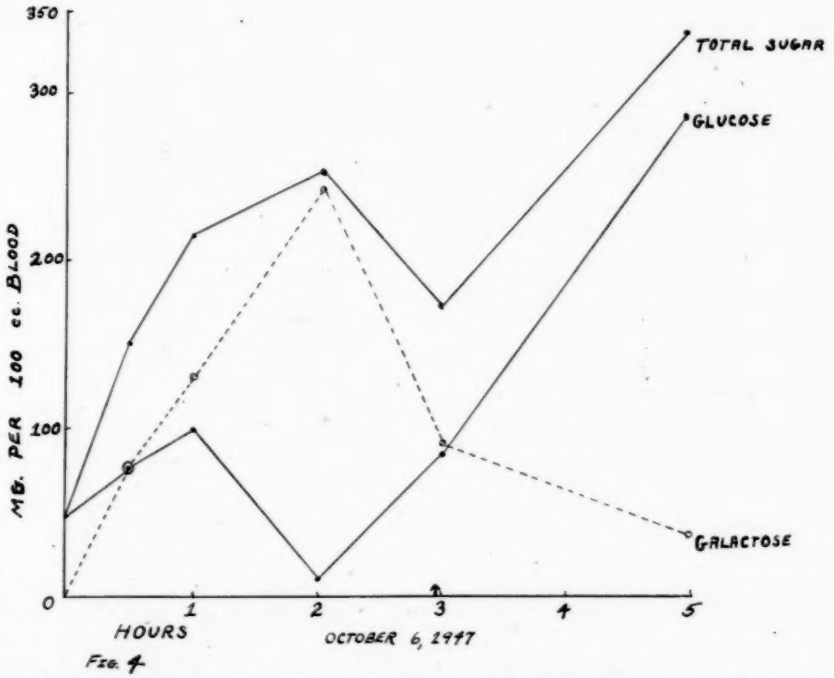

Fig. 4.—Values for total blood sugar, glucose, and galactose after the ingestion of 1.75 Gm. of galactose per kilogram of body weight.

COMMENT

Another case of galactosemia is reported. Our patient was characterized by failure to gain weight and grow properly, general underdevelopment, enlargement of the liver, melituria (galactose) albuminuria, anemia, and cataracts. Removal of galactose from the diet resulted in improvement of all abnormalities except for hepatomegaly, which showed but slight change. Our case differs but little from those previously described.

In several of the cases reported, careful studies have been made on carbohydrate metabolism, which we have attempted to duplicate. From these studies the following conclusions may be drawn: (1) There is a normal glucose tolerance curve. (2) There is an abnormally high galactose tolerance curve. (3) The two sugars, glucose and galactose, have mutually antagonistic effects upon one another. Attempts to explain the pathologic changes occurring in this condition have been made by several workers. Mason and Turner feel that the primary trouble is a lesion or functional disturbance of the liver that lowers

Fig. 5. Fig. 6.

Fig. 5.—W. J., aged 3½ months, before therapy.
Fig. 6.—W. J., aged 6½ months, after three months of milk-free diet.

the ability of the organ to convert galactose into glycogen without seriously impairing the other functions of the liver. "Milk in the diet results in galactose reaching the general circulation; the circulating galactose maintains the total blood sugar at a level high enough to stimulate the mechanism for lowering the blood sugar, and this mechanism, unable to act satisfactorily on the galac-

tose, acts excessively on the dextrose and causes the storage of abnormally large amounts in the liver. When milk is withdrawn from the diet, galactose disappears from the blood; the level of the blood dextrose again rises, and gradually the excess of stored glycogen is discharged from the liver." This explanation depends on the validity of the assumption that it is the height of the total blood sugar and not that of dextrose alone which sets in motion the mechanism for lowering the amount of blood sugar.

These same authors believe the other findings, such as anemia, osteoporosis, and elevated van den Bergh, are secondary, not primary, and in some way related to the continuous presence of galactose in the circulation. This they explain by (1) the diffusion of galactose throughout the body and its interference in some way with normal metabolism, or (2) a relative dextrose starvation, interfering with normal cellular activity. The albuminuria, they feel, is similar to that found in diabetic children when first observed, and which also disappears when they become sugar-free as the result of treatment.

Bruck and Rapoport raise several objections to Mason and Turner's hypothesis: first, that hypoglycemia per se, as seen in glycogen storage disease and hyperinsulinism, does not produce symptoms similar to those of galactosemia; and second, that hypoglycemia does not appear to be an essential feature of the disease. In their patient and in others the hypoglycemia was only transient, occurring only during a galactose tolerance test.

Bruck and Rapoport suggest a toxic effect of galactose on the various tissues as a cause of the pathologic changes noted in this disease.

Norman and Fashena agree with Mason and Turner that galactosemia is due to failure of the body to convert galactose into glycogen and that the associated manifestations are due to a relative dextrose starvation.

Mellinkoff feels the defect is due to galactose or a polymer of galactose being stored in the liver and causing injury to the liver with resulting hepatic dysfunction.

Most recently Goldbloom and Brickman suggest that the high blood level of galactose interferes with the absorption of glucose from the intestine and this causes the low blood glucose when lactose is being fed.

The presence of cataracts associated with this condition and the reversibility in some cases is of interest. In 1935, Mitchell and Dodge, in experiments on the effects of high carbohydrate diets, found that on diets containing 70 per cent of lactose, rats regularly developed cataracts, whereas equal amounts of starch, maltose, dextrin, or sucrose had no such effect. Subsequently it was proved that galactose, not lactose per se, was the offending compound. In some of the rats in which the lesion did not progress to the stage of complete opacity, the lens became completely clear.

SUMMARY

1. Another case of galactosemia, in a 2½ month old infant, has been reported and the literature reviewed.

Our case had the features common to all the other cases—namely, failure to gain weight and develop properly, melituria, and albuminuria. In addition,

our patient showed cataracts, which have been described in 50 per cent of the other cases. The reducing substance was identified as galactose. By the removal of lactose from the diet, there was subsidence of all the pathologic signs and symptoms except for the enlarged liver.

2. Carbohydrate studies were done, and results similar to those of previous workers were reached; these were a normal glucose tolerance curve, a high galactose tolerance curve, and antagonistic effects of glucose and galactose upon one another.

3. Theories of the mechanism of galactosemia have been reviewed.

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A STUDY OF PHYSICAL ACTIVITY IN JUVENILE DIABETIC PATIENTS

ROBERT L. JACKSON, M.D., AND HELEN G. KELLY, M.S.
IOWA CITY, IOWA

EXERCISE was known to be an important factor in the treatment of diabetes mellitus long before the discovery of insulin. Since the discovery of insulin and the advances made in its refinement and modification, along with the recent rapid advances in our knowledge of nutrition, exercise as a factor in the treatment of diabetic patients has received little attention. The objective of our clinic in the management of diabetes mellitus is to maintain normal physiologic conditions. In most clinics the diabetic child is permitted to maintain a mild glycosuria as an insurance against shock. In this clinic, however, this state would be considered a level of only fair control. When the level of control requires that the child remain aglycosuric, the effects of exercise become more apparent.

In 1940 the method was described by this clinic for stabilization of children with diabetes mellitus.[1] The regimen outlined has been effective, and a large number of children have been able to maintain excellent regulation over extended periods of time. The importance of physical activity as a factor in maintaining stability became more apparent as the children were observed under home management. During vacation periods with greatly increased physical activity, insulin reactions occurred unless the insulin dosage was reduced or the food intake increased. Earlier, the families were advised to decrease the insulin. This resulted in less than expected weight gains during periods of the year when physical activity was strenuous. Histories obtained from the families revealed that insulin reactions were frequently associated with periods of excessive physical activity. Marked reduction of insulin requirement was common during the summer months or during periods of heavy work. A few children were able to maintain regulation for periods of time without the use of insulin. Soon it became obvious that it was better to give additional food rather than to decrease the amount of insulin in order to compensate for increased physical activity. The families were instructed to note variations in physical activity in their daily record books. They were advised to give small additions of food at meals or at the time of exercise. Clinically, the children were observed to maintain better regulation when the food was given at mealtimes. A graphic chart has been made for each diabetic child in our clinic from the home records kept by the families. These records include insulin requirement, growth, dietary intake, glycosuria, insulin reactions, infections, major emotional disturbances, and variations in physical activity. These records have been carefully studied to learn more about exercise as a factor in diabetic regulation of children.

From the Department of Pediatrics, State University of Iowa.

This report on physical activity of diabetic children comprises two sections: (1) the effect of short periods of physical activity of children observed under experimental conditions, and (2) the effect of free activity of children observed in the outpatient clinic.

SECTION 1: ACTIVITY UNDER EXPERIMENTAL CONDITIONS

In 1941, as part of the requirement for a master of science degree, a graduate student of nutrition studied the effect of physical activity on the blood sugar values of diabetics under various levels of diabetic control during a one-hour experimental period.[2]

Method of Study.—The group was composed of one normal child, seven hospitalized patients, and ten outelinic patients whose diabetes was under various levels of control. Blood sugar values were determined on these eighteen subjects, who ranged in age from 3 to 22 years.

The observation period of physical exercise was in the morning between 9:30 and 10:30 o'clock, three hours after the morning dosage of insulin and approximately two and one-half hours after breakfast. Three types of physical activity were studied. They were: strenuous—running or bicycling; moderate—walking, skipping, swinging, jumping rope intermittently, and playground activity; minimum—reading, sitting, and lying down.

Finger-tip blood* was drawn one-half hour before the physical activity observation period, immediately preceding it, at the mid-period, at the completion, and one-half hour after completion.

Findings.—The following is a brief summary of the findings as reported in the thesis:

Regardless of the type of activity the blood sugar values of the one normal child in the study group were within normal range. When her blood sugar values were over 100 mg. per 100 ml. at the beginning of the physical activity study period, the values all decreased for each of five moderate exercise periods with a mean change of −17.6 mg. per 100 ml.; when her blood sugar values were less than 100 mg. per 100 ml., her blood sugar values increased for each of two moderate exercise periods and decreased very slightly for one period with a mean change for the three periods of 11.3 mg. per 100 ml.

The three subjects in excellent diabetic control had blood sugar values which varied from 59 to 104 mg. per 100 ml. one-half hour before exercise and from 79 to 120 mg. per 100 ml. one-half hour after the completion of exercise. Six patients under good control were observed for a total of nine study periods. During or after minimum, moderate, and strenuous physical activity there were no marked fluctuations in the blood sugar values. (See Figs. 1 and 2.)

No significant alterations in blood sugar values were revealed after short periods of moderate exercise in patients when the disease was fairly well controlled. Patients under fair control who had elevated postprandial blood sugar levels had a progressive lowering of blood sugar values, but no rapid lowering.

*A micromodification of the Folin-Wu method was used for estimation of sugar content, and the Somogyi method for precipitation was employed.

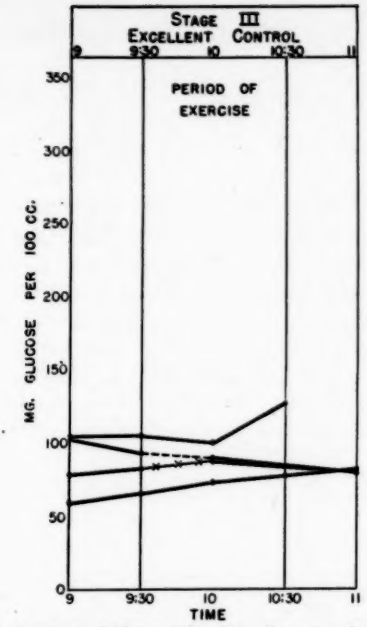

Fig. 1.—Blood sugar changes during and after the experimental period of physical activity from 9:30 to 10:30 A.M. of patients whose diabetes was under excellent control. The blood sugar values were not noticeably affected by the exercise. x x x x indicates minimum degree of physical activity, —moderate, and - - - - strenuous.

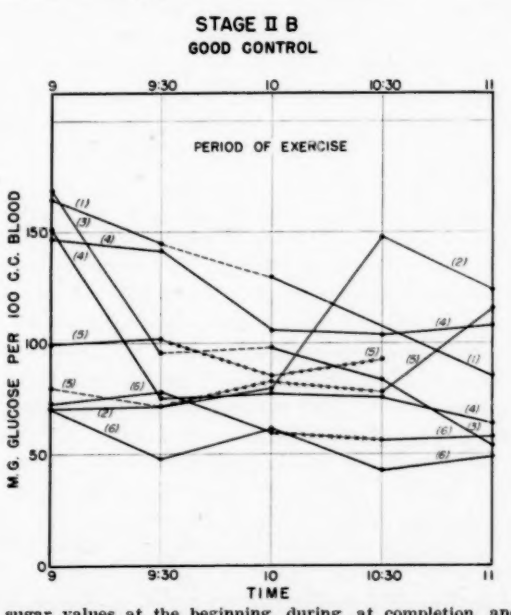

Fig. 2.—Blood sugar values at the beginning, during, at completion, and one-half hour after completion of the experimental period of physical activity of patients whose diabetes was under good control. (Symbols same as in Fig. 1.) The observations were made for six children for a total of nine experimental periods. An ascending curve during moderate activity was shown by patient (2), who was used to manual labor. Otherwise minimum, moderate, or strenuous physical activity caused no great variation in blood sugar values.

In all stages of management of children with diabetes mellitus, during or after short periods of moderate to strenuous physical exercise there tends, with few exceptions, to be a lowering of the blood sugar values. The greatest decrease in blood sugar values was for those who had elevated blood sugar values at the beginning of the observation period of physical activity.

During experimental exercise periods the blood sugar values of the stabilized diabetic children decreased gradually, and no child experienced an insulin reaction during the hour of exercise or immediately after it. This sample of seventeen diabetic subjects is small, but the consistency of the finding of a gradual lowering of the blood sugar value during increased exercise suggests that if a child has been stabilized and is maintaining a good level of diabetic control, he can compensate for short periods of unusual exercise ranging from moderate to strenuous by taking an amount of extra food at mealtimes commensurate with the increased need.

One patient in the stage of metabolic recovery was studied for two separate periods of moderate exercise. He was rapidly gaining weight, and his daily insulin requirement was decreasing. His blood sugar values were low, and during the experimental exercise periods he complained of weakness and had to rest before the end of one of the periods.

SECTION 2: FREE ACTIVITY

Type of Muscular Exercise Taken by Diabetic Children and Adolescents Living in Rural Communities.—The muscular exercise taken by the young diabetic children under the supervision of the clinic of Children's Hospital was for the most part determined by the child's inclinations and the circumstances of his home life and school program. The children were, however, instructed to participate in activities that would not conflict with the regularity of their diabetic regimen.

A number of children have been specific in recording in their daily record books the amount and kind of activity of consequence in which they participated over and above the routine of an ordinary day. Several boys particularly have been able to manage a great deal of activity without loss of diabetic control. One high school boy (R. G.) after school hours manages to practice basketball or band or orchestra or plays for dancing, and in the summertime has detasseled hybrid corn eight to nine hours a day. Another boy (R. S.), in junior high school, lists as his extra activities one to three hours of basketball practice, baseball, swimming, bicycle riding, boxing, mowing lawns, and working in a bowling alley three to four hours. A grade school girl (A. H.) carefully listed her extra activities. They included housework, shopping, sleigh-riding, baseball at recess, flower picking, parties, and playing in the snow. A high school girl (M.D.) listed her extra activities as housework, walking to town, gymnasium class, and social dancing in the evening. As a rule the children did not record so much specific detail as those just mentioned, but stated in general whether the exercise was usual, more, or less, for school or vacation time. This review, however, of the detailed records is helpful in evaluating the amount and strenuousness of

activity of some diabetic children and adolescents residing in rural or semirural areas. The inactivity also is recorded. Bed rest probably represents the least daytime activity. Many indicate inactivity as less than usual with the explanation of a rainy day or very cold day.

Constancy and Fluctuations in Exercise in Relation to Control of Juvenile Diabetes Mellitus.—In general the school routine tends to maintain the exercise of children at a fairly constant level from day to day during the school months. For a few diabetic children the variation in the amount of exercise for school days and for week ends is great enough to reflect itself and needs compensation. In the spring of the year when outdoor play and work start, for many the amount of exercise increases and is more variable from day to day. With the coming of vacation and still more activity, it has been observed that the well-regulated patient will have shocks unless some compensation is made. In the records there are instances of shock after periods of strenuous exercise such as swimming for a few hours and active play for a day at a picnic. There also are instances of shock after periods of gradually increasing exercise over a period of days such as the change from winter to spring farm work. Glycosuria invariably resulted when the amount of exercise was less than usual. These are typical reactions of patients who have not learned or have not heeded the advice to compensate for marked changes in exercise.

We have observed that some intrinsic characteristic of a few well-regulated patients makes them tolerate inconstancies in exercise better than average. For example, N. P., a girl whose diabetes has remained in excellent control, was able to exercise two days a week in her physical education classes without decreasing the amount of insulin or increasing the amount of food.

Illness can cause fluctuations in physical activity. The change from bed rest to usual activity has been observed to precipitate a shock when care is not used at this time to compensate for increased exercise.

Exercise in Relation to Age and Sex of the Diabetic Patient.—The age and sex of the child are factors to be considered in evaluating exercise. The games and play of children involve a great amount of physical exercise. The responsibility that the young child can assume to recognize the early signs of shock is at a minimum. The amount of reserve glycogen is relatively less than for the older child.

When boys and girls become adolescent the differences in strenuousness of the activity of the two sexes are accentuated. After puberty, girls tend to spend more of each day in less strenuous leisure, while the boys frequently spend more time in greater muscular activity, both in work and in leisure. The lack of exercise in many diabetic adolescent girls is a major factor for the rather frequent occurrence of obesity in this age group.

Compensation for Changes in Exercise.—The home records confirm the hospital experimental study that short periods of exercise, such as the intermittent exercise of a gymnasium class, of farm or household chores, or of walking, are tolerated by the well-regulated diabetic child. The basic diet, if adequate, will take care of minor fluctuations in daily exercise.

For an occasional period of very strenuous exercise, such as basketball practice for two hours or swimming vigorously off and on for two hours, some compensation should be made to avoid precipitating a shock. If a meal is to be eaten shortly after the exercise, extra food in proportion to the change in exercise should be given at this meal. If the exercise has been taken in the early evening, a lunch may be eaten during the evening or before going to bed.

If the child or young adult changes his whole pattern of exercise, as from school to vacation or from winter to spring farm work, the first adjustment in his regimen should be an increase in his basic diet commensurate with his increased physical activity. Earlier in our regulation of diabetic patients we lowered the insulin at times of prolonged increased activity. This method gave the apparent advantage of a lower insulin requirement, but it resulted in loss of body weight. C. V. illustrates this method of compensating for more exercise during vacation periods (Fig. 3). For three and one-half years this adolescent boy consistently kept an accurate home record of his insulin dosage. He reported that, because of increased activity at a summer camp in 1939, from mid-June to mid-August, he had to decrease considerably his insulin dosage to avoid insulin reactions. During the school months there was lessened activity necessitating a steady rise in insulin. During the spring months there was more activity, which was accompanied by a steady decrease in insulin need. During the first June spent at camp there were frequent mild insulin shocks associated with increased activity and a decided drop in insulin requirement, so that during mid-vacation he was able to decrease the daily insulin dosage by 27 to 32 units. Concurrently with this decrease in insulin, there was an increase of 187 calories in his diet and a weight loss of 7 pounds. The patient was usually aglycosuric, and only occasionally excreted a minimum amount of sugar in the urine. The glycosuria was usually associated with mild infections, which were immediately controlled. During a short spring vacation, in which activity was increased, there was a slight decrease in the insulin need. During the summer camp periods of 1940 and 1941 there were rapid decreases in the insulin requirement, but no shocks were recorded. The patient had learned from the experience in 1939 that increased activity reduced the insulin requirement.

C. H., a preschool child, also shows the influence of changing exercise on weight (Fig. 4). This little girl was inclined to a great deal of runabout play, and when the weather permitted she played practically the whole day outdoors except for her nap time. This accounts for her marked seasonal variations in exercise. Not until her basic diet was raised in the spring of the year did she make the expected weight gains. This condensed chart of her diabetic record reflects changing insulin requirements with seasonal variations in physical activity and with fairly frequent upper respiratory infections, so common to this age period. C. H. was treated early, her disease was moderately severe, her diabetic regulation was excellent, and she had a good tolerance of exercise. This child did not experience clinically significant shock, but on two occasions when her daily exercise was increasing, mild symptoms of shock were present and compensation was immediately made.

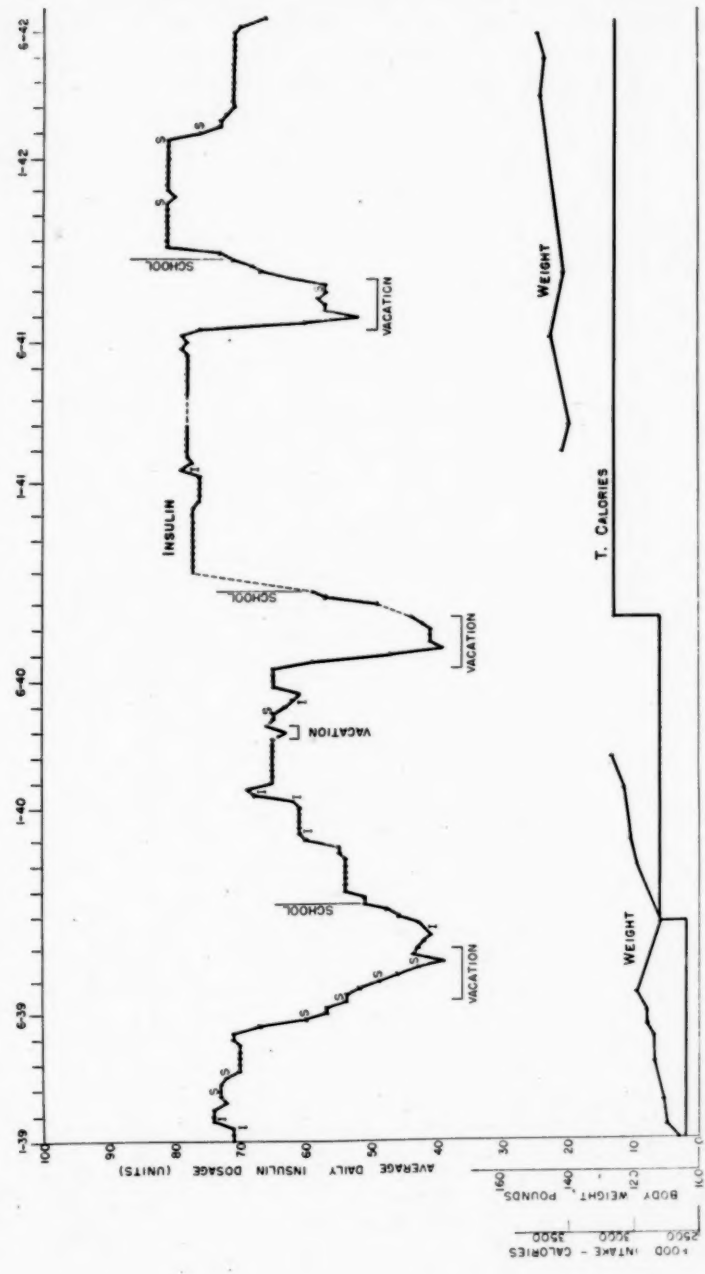

Fig. 3.—Daily insulin dosage of a boy, C. V., whose diabetes was under good control over a three and one-half year period, including school years and vacations spent at a boy's camp. Regular exercise taken over a period of days and weeks resulted in a decided decrease in the insulin requirement. Return to school and the sedentary life necessitated sharp increases in insulin dosage. (I) represents an infection, which is usually followed by increased insulin dosage. (S) represents shock, which usually accompanied increased exercise and necessitated a decrease in insulin dosage. Weight loss was concurrent with increased activity without an increase in basic diet or extra food. The dotted line (----) represents the period in which data were not obtainable.

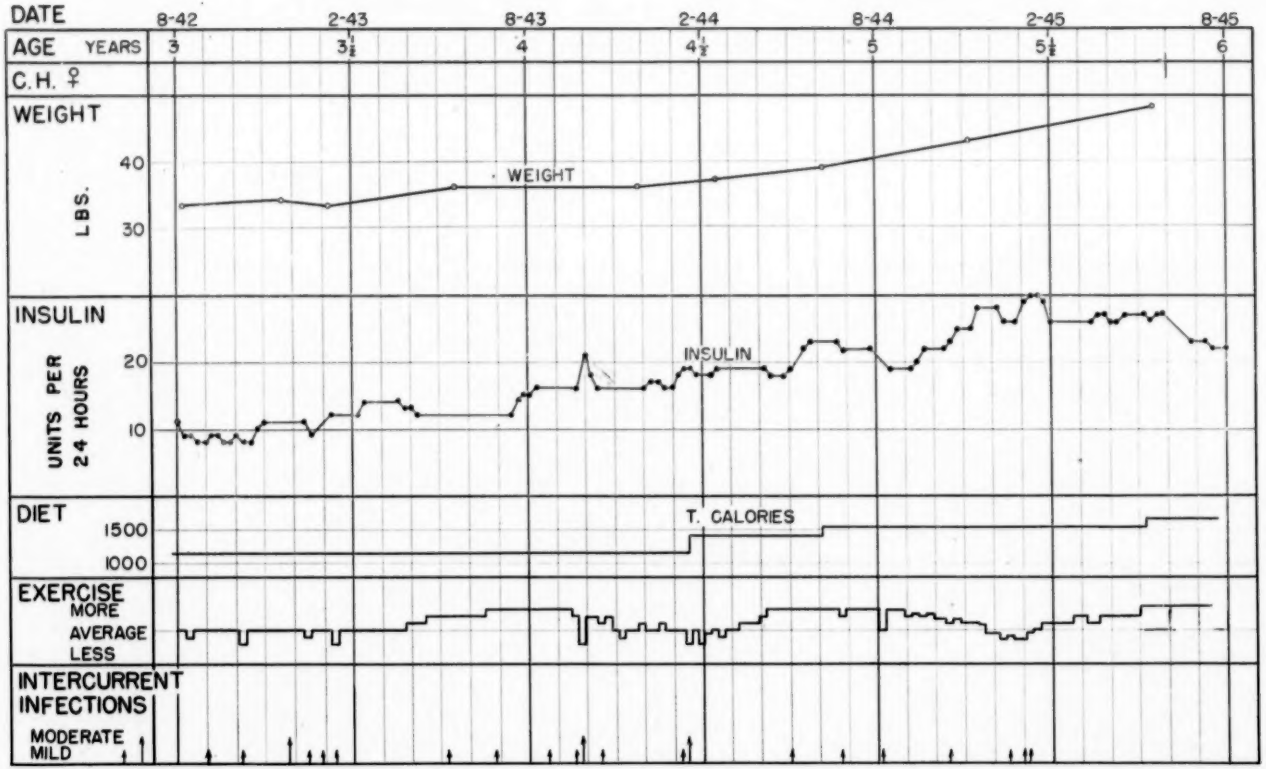

Fig. 4.—Shows three years of diabetic regulation under home conditions of a preschool girl, C. H., under excellent diabetic control. Her urine was free from sugar except for very occasional traces. There were no clinically significant insulin reactions, but on two occasions she had mild symptoms of shock with increased exercise.

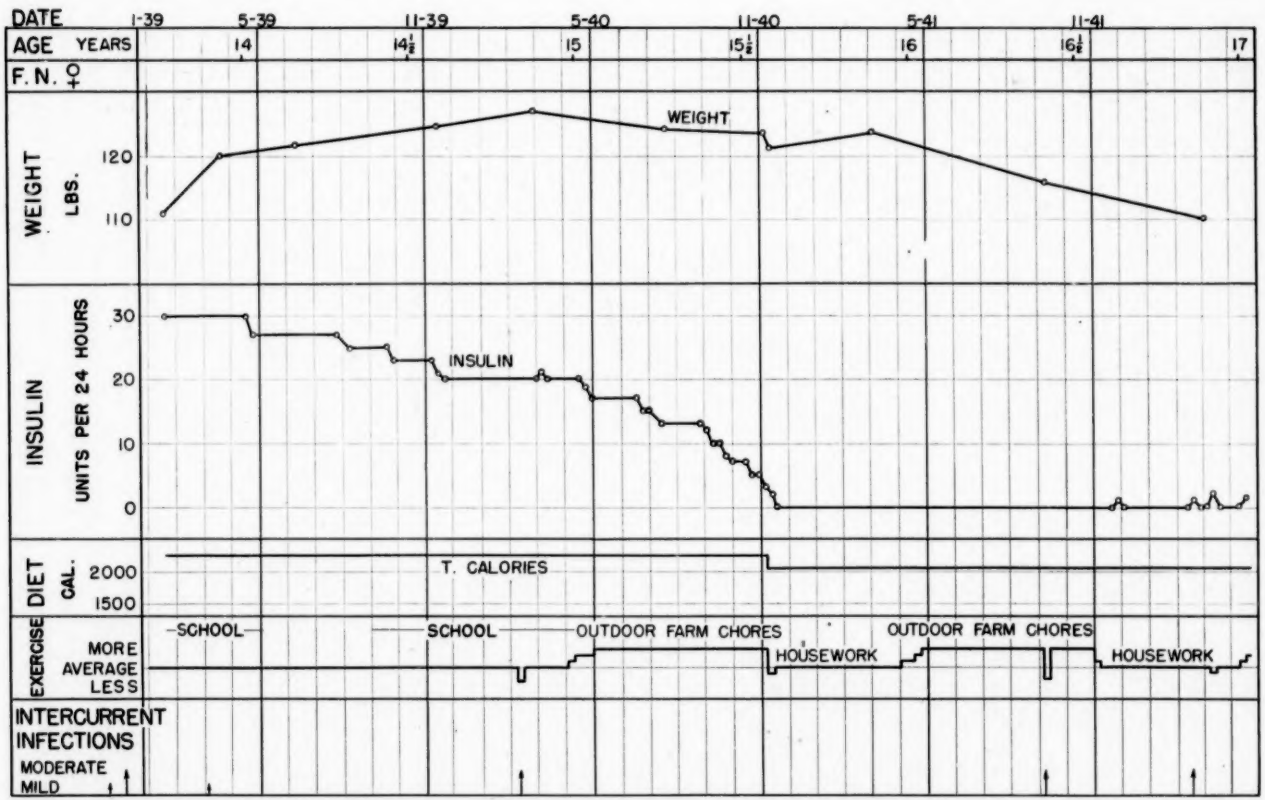

Fig. 5.—Shows three and a quarter years of diabetic regulation of F. N., a girl 13 years and 8 months of age at onset of the disease. Her diabetes mellitus was brought under excellent control shortly after onset, and at the time of her dismissal from the hospital she was taking 30 units of insulin daily. The course of her insulin requirement and weight changes in relation to her dietary, physical activity, and infections are presented.

F. N., a 13-year-old girl, had good health up to three weeks prior to her admission to the hospital (Fig. 5). At that time she had a cold, polyuria, polydipsia, increased appetite, and was lethargic. Three days before admission, she complained of a slight earache and was taken to a doctor. He found sugar in the urine and made a diagnosis of diabetes mellitus. At the hospital the child was stabilized on a total of 30 units of regular insulin and was discharged Jan. 19, 1939.

The disease in this girl was brought under control early; it remained mild and responded well to treatment. The child was aglycosuric at all times except during infections. This girl, in spite of efforts to change her attitude toward her disease, was ashamed to be a diabetic and was opposed to taking insulin. In the spring of 1940 she began exercising a great deal, doing housework and farm chores. She reduced her daily insulin dosage from 25 units until she was taking no insulin. Four urine specimens were examined daily. The specimens remained sugar-free except for very occasional traces. Exercise was increased if mild glycosuria occurred. She lost 3½ pounds in weight. She did not return to school in the fall of 1940, and in November when she visited the clinic she was instructed how to decrease her diet about 200 calories so she would not require insulin during the winter when she was exercising less. During the spring and summer of 1941 she again exercised a great deal; she took no insulin and remained on the lower caloric intake per day. She lost weight.

During the first fourteen months after this adolescent girl was discharged from the hospital, when she was taking insulin and had a larger diet and less exercise, her weight increased and in relation to the average weight for her age was a plus two-thirds standard deviation.[3] Her height was average for her age. Exercising and decreasing her diet and insulin reduced her weight to two-thirds standard deviation below the mean for her age during the course of the next two years.

Postinfection can be considered a critical time for diabetic patients. At this time the patient is changing from decreased activity or bed rest to normal activity. During active infection, the insulin dosage is raised to control the glycosuria due to the infection. When the infection clears up rather abruptly, the child feels better and exercises more. Unless the patient is watched closely at this time and the insulin correctly adjusted, a shock may easily be precipitated. A review of all of our well-regulated patients as to cause of shock revealed that 26 per cent of the severe shocks were postinfectional.

Prior to recognizing the importance of physical activity as a factor in diabetic management, shocks associated with increased activity were commonly encountered. The insulin dosage frequently was not decreased until the child had mild symptoms of shock. Physical activity was not routinely recorded in the home records prior to the time advice was given to make compensation for variations in physical activity. But the charts of the children observed at this earlier period showed fluctuations in insulin requirement and insulin shocks similar to those demonstrated for C. V. (Fig. 3). A review of the home records of twenty-three well-regulated patients since advice was given to compensate

for increased physical activity showed that in a total of 1,062 patient-weeks the incidence of shocks was only one reaction every six months. Eighty-three per cent were mild reactions.

DISCUSSION

Exercise is essential for good wholesome living and physical development of the young, so it should be provided for in their diabetic management. When instructing a juvenile diabetic patient in his diabetic management, an understanding of the daily routine and physical activity is necessary. A good over-all picture of the child's activity and of the factors that control or influence his activity should be obtained. A review of our diabetic progress charts for the home regulation period shows the following factors pertinent to the evaluation of exercise:

(1) Age of the child, (2) residence (rural or town), (3) distance from school, (4) physical training in school, (5) participation in sports, (6) Saturday and Sunday activity, (7) summer or vacation activity, (8) inclination to strenuous, moderate, or light muscular work or play. The study of periods of experimentally controlled physical activity at known intervals after meals and insulin administration demonstrated that such exercise is usually accompanied by decrease in blood sugar. In well-regulated children the decrease of blood sugar was small and was not accompanied by evidence of insulin shock. The study of the diabetic child or young adult in home and school situations indicates similar effects from short periods of unusual exercise; there was evidence of insulin shock from long periods of unusual exercise and from periods of increasing exercise lasting over days or weeks.

Insulin is necessary for the storage of carbohydrates. The hospital studies showed that by two and one-half hours after breakfast the normal child and the majority of the well-regulated diabetic children had normal blood sugar values and that most of the carbohydrate of the meal had been used or stored. Energy expenditure per hour varies under different conditions of muscular activity.[4] A child weighing 100 pounds uses 43 calories per hour while sleeping, and 422 calories when walking very fast for an hour (5.3 miles).

Sometimes several disturbances are present concurrently with changes in exercise, as an infection or an emotional upset. It is impossible to estimate how much each disturbance or change affects the insulin requirement of the child. Two or more disturbances could be present concurrently for longer periods also, as, for example, the change from the emotional stress and less physical activity of school life to the relaxation and greater physical activity of vacation. One mother reported this condition was apparent at the beginning of vacation when her 13-year-old daughter, M. T., had had a conflict with her teacher and had worked under tension that year in school. The fact that some children lost weight or did not gain during the summertime indicates that exercise is probably the most important factor and not the decreased emotional strain, in lowering the insulin requirement.

In our study of exercise under home regulation, we have limited our evaluation to the well-regulated patients because these subjects generally keep better

records than those who maintain a lower level of diabetic control. It is obvious that a well-kept record is essential when the relation of exercise to diabetic regulation is being studied.

Presumably when the well-regulated diabetic child exercises more than usual, he utilizes his glucose directly for energy, and consequently he has an excess of insulin available to convert glucose into glycogen. The loss of glucose from the blood, both by utilization and storage, easily may result in hypoglycemia. If the patient has mild diabetes mellitus requiring only a small amount of exogenous insulin, his ability to compensate will be enhanced by the depression of the endogenous insulin. On the other hand if the disease is severe, requiring a large amount of exogenous insulin, the patient will have a smaller threshold of safety.

It has been observed that if the diabetes of the child is well regulated and he maintains good control, later when he becomes more mature physically and mentally he is freer from shocks of all types. The adolescent or young adult learns to judge his tolerance for exercise and his need to compensate by eating extra food for unusual periods of strenuous exercise. However, the adolescent must be advised when and how much extra food he needs, in order to prevent erratic and excessive compensation and poor dietary habits. It is preferable that extra food be eaten at mealtimes. For the young adult, the privilege of eating socially after an evening party, dance, or game has psychologic and social advantages and is provided for in our regimen.

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GRAPHS OF THE HEAD CIRCUMFERENCE OF THE NORMAL INFANT*

HENRY K. SILVER, M.D., AND WILLIAM C. DEAMER, M.D.
SAN FRANCISCO, CALIF.

THE periodic measurement of head circumference is an important item in the routine examination of the infant, and is an aid in the diagnosis of various pathologic conditions. Not only is the size of the circumference itself of interest, but knowledge of its rate of increment is of even more value. The comparison of these data, especially the rate of increment, with normal values, may be of considerable aid in the early recognition, or ruling out, of the presence of such conditions as hydrocephalus, retarded mental development, or premature closure of cranial sutures. However, due to the difficulty of interpreting the data hidden in lengthy tables now used to determine whether the increment of growth in a given case is within normal limits, this important step in the physical examination of some children is often neglected. To simplify the method of calculation, graphs were devised and are presented here for use in the clinical appraisement of the child from birth to 2 years.

In some instances the size of the head is such as to lead to a suspicion of hydrocephalus. Adequate interpretation of the data, however, may reveal simply a normal rate of growth of an unusually large head. The latter is frequently found to be a familial characteristic. On the other hand, an abnormally rapid increase in size may be demonstrated in some cases and thus confirm the suspicion of hydrocephalus earlier than would otherwise have been possible. The progress of the condition may then be followed, and in certain cases a flattening of the gradient into a normal slope may indicate the establishment of an equilibrium and a cessation of abnormal growth. Since certain types of hydrocephalus may occasionally be amenable to surgical treatment, early recognition of abnormal increase in the size of the head may permit the more prompt institution of therapy.

The knowledge that growth of the head is taking place at a subnormal rate may confirm a suspicion of mental retardation, whereas demonstration of a normal increment may go far to allay fears that a small head has similar implications. In other instances the diagnosis of premature closure of cranial sutures may be established at an early stage of the condition if cessation of normal growth is noted. Recent reports by Simmons and Peyton[1] and by Faber and Towne[2] have re-emphasized that early recognition is of the greatest importance, since the results of surgical treatment depend, in a large measure, upon the promptness with which this treatment is initiated. Changes in the growth pattern of the head, as compared to the normal, may indicate the seriousness of the

From the Department of Pediatrics of the University of California Medical School.

*Copies of the composite graph of head circumference for males and females may be obtained from Pacific Rotoprinting Company, 306 Twelfth Street, Oakland, Calif.

condition before marked abnormality of shape, loss of vision, retardation of mental growth, or other sequelae have occurred.

During the past twenty-five years, many reports have been published giving the size of the head circumference at various ages. The data from those reports[3-18] which contained measurements at several age periods and which were limited to normal, healthy, white children, of predominantly Northwest European ancestry, were incorporated to make graphs of head circumference for male

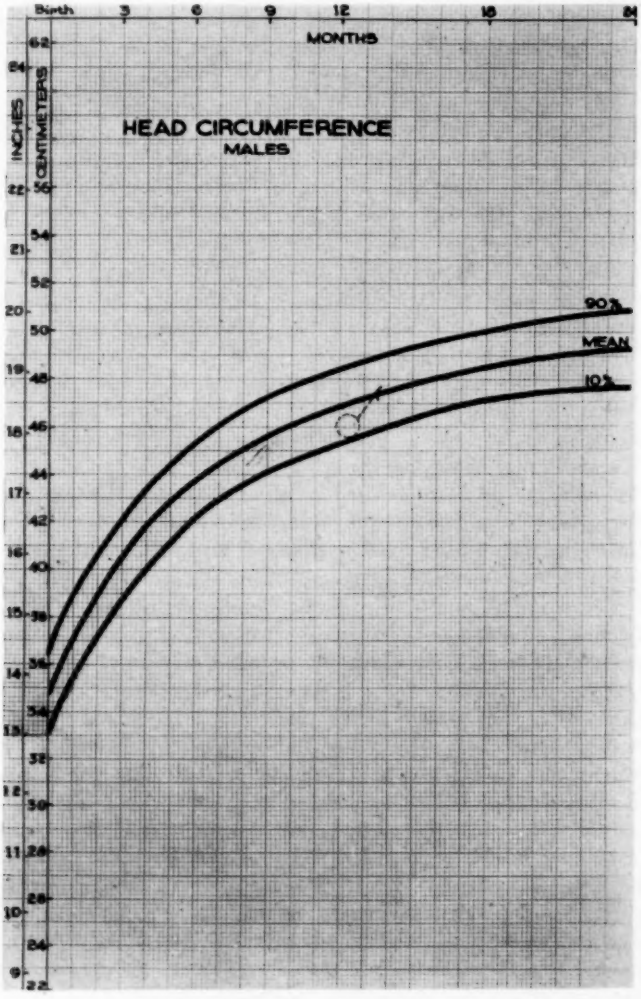

Fig. 1.—Graph of head circumference for *male* infants. (Based on data of normal, healthy, white children of predominantly Northwest European ancestry.)

(Fig. 1) and female infants (Fig. 2) ranging in age from birth to 2 years. A composite of these two groups (Fig. 3) has been found to be especially useful for reference in the office, clinic, or hospital ward.

In using the graphs it should be remembered that 20 per cent of all measurements (the largest 10 per cent and the smallest 10 per cent) will fall outside the 10 and 90 percentile lines. In this group, knowledge of the rate of increment is of particular interest since it will often reveal normal rate of growth of the head when the original measurement suggested some abnormality.

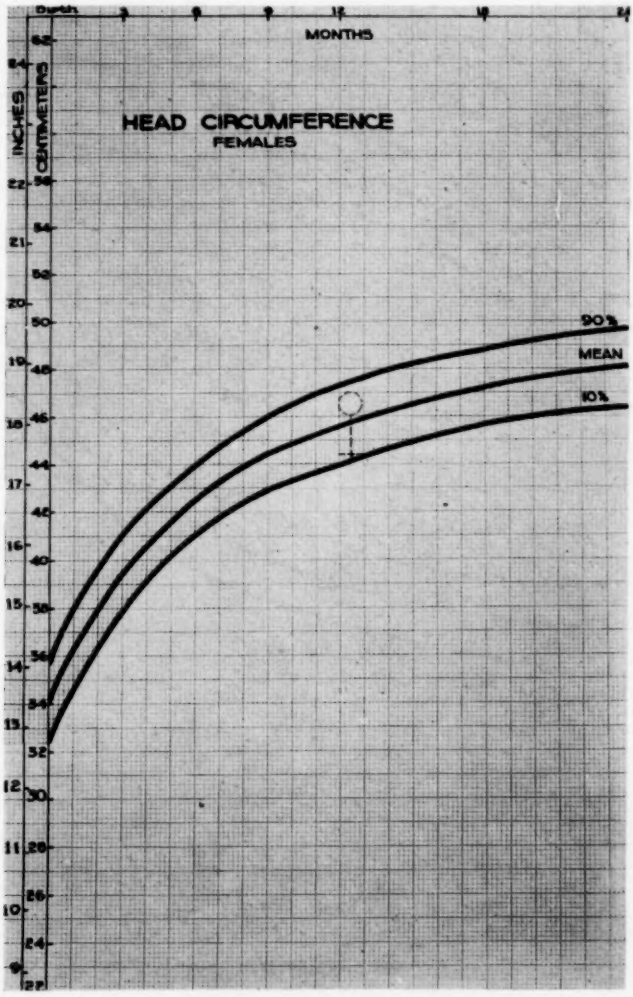

Fig. 2.—Graph of head circumference for *female* infants. (Based on data of normal, healthy, white children of predominantly Northwest European ancestry.)

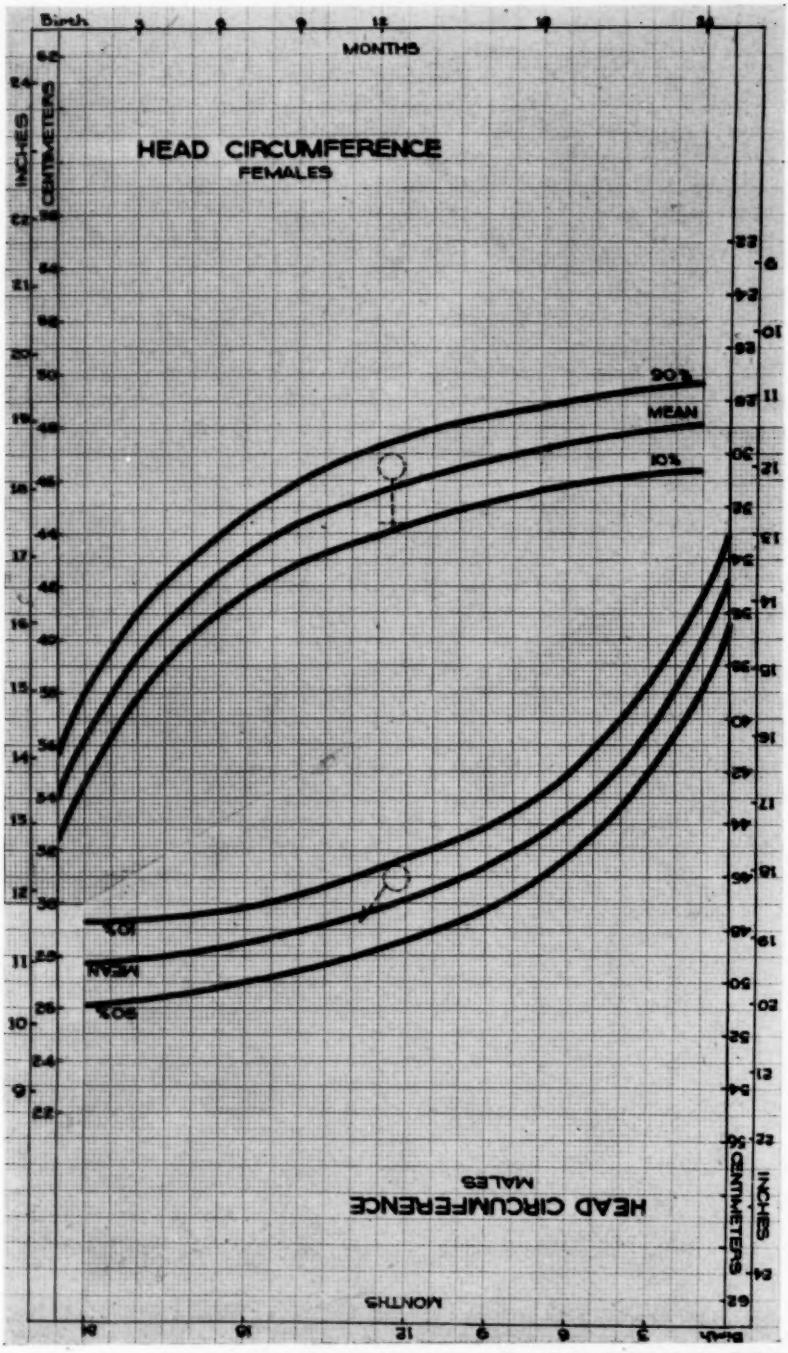

Fig. 3.—Composite graph of head circumference for *male* and *female* infants for desk use. (Based on data of normal, healthy, white children of predominantly Northwest European ancestry.)

SUMMARY

To aid in the clinical appraisement of the normal infant and in the early recognition of hydrocephalus, retarded mental development, or premature closure of the cranial sutures, graphs of the head circumference of infants are presented, which offer a convenient means of comparing with normal values both single measurements of circumference and the increment of growth of the head.

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ARTHRITIS, CONJUNCTIVITIS, AND URETHRITIS (SO-CALLED REITER'S SYNDROME) IN A FOUR-YEAR-OLD BOY

ALFRED L. FLORMAN, M.D.,* AND HAROLD M. GOLDSTEIN, M.D.
NEW YORK, N. Y.

IN 1916, during World War I, Reiter[1] described a patient in the German army who developed arthritis, conjunctivitis, and urethritis following an episode of diarrhea. Since then a number of other instances, almost all in adult males, have been reported. Most of these have been recently reviewed by Vallee.[2] The syndrome usually begins with either urethritis or purulent conjunctivitis. Dysuria and frequency of urination are associated with the urethritis. The conjunctivitis is occasionally followed by keratitis, iritis, and iridocyclitis. Later the joints, particularly those of the ankle and knee, become acutely inflamed and tender. This arthritis is often migratory, but may be limited to a single joint. Hydroarthrosis is common, but destructive changes in the joints are infrequent. There is usually a low-grade fever, a moderate elevation of the leucocyte count, and an increase in sedimentation rate. The clinical course is often characterized by remissions and exacerbations but usually terminates favorably in two to four months. Although it was in 1942 that the first account of this syndrome appeared in the American literature,[3] many patients among our troops during World War II were recognized as presenting this triad of symptoms.[4-6]

To some observers, Reiter's syndrome is not an etiological entity (see references of Young and McEwen[6]); however, to most others there appears to be a relationship to some definite infection. Although a spirochete was demonstrated in the blood of Reiter's patient,[1] most observers have tended to disregard this finding. In recent years attention has centered about an association with dysentery bacteria,[5] pleuropneumonia organisms,[2] or some as yet not clearly defined viruses.[7, 8]

It is the purpose of the present communication to give the case history and results of the bacteriologic, virologic, and immunologic investigations in a 4-year-old boy who became ill and developed the classical Reiter's syndrome. It is believed that this is the first recorded instance of this disease in a child.

CASE REPORT

R. K., a 4-year-old white male child, was admitted to The Mount Sinai Hospital Pediatric Service on Aug. 16, 1947, because of inflamed eyes, a swollen painful right knee, and painful urination of two days' duration.

Family History.—Both parents had seasonal hay fever. A sibling, 10 months old, was living and well. The family history was otherwise noncontributory.

Past History.—The child's birth, early growth, and development were normal. Except for frequent upper respiratory infections and an uncomplicated attack of measles he had been well. One month prior to admission, during a routine physical examination, a cardiac murmur was noted. There was no antecedent history of rheumatic or cardiac symptoms.

From the Pediatric Service of Dr. Murray H. Bass and the Division of Bacteriology, The Mount Sinai Hospital, New York City.

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Present Illness.—One week prior to admission the patient had watery diarrhea. However, the stools did not contain blood, mucus, or pus, and were normal after three days. For two days preceding admission, there were urgency, frequency of urination, and dysuria. At the same time both eyes were observed to be inflamed. On the morning of admission the child appeared feverish, and his right knee was swollen and painful. He refused to walk or stand. There were no complaints referable to any other joints. Although the mother had had diarrhea at about the same time as the child, neither she nor the other members of the family showed symptoms similar to those presented by the patient.

Physical Examination.—The child appeared to be acutely ill and moderately febrile. He was normally developed, but somewhat pale and underweight. The rectal temperature was 102° F., the pulse was 96, respirations 20, blood pressure 98/60 (R.A.). His weight was 31.4 pounds (14.2 kg.). There was a bilateral purulent conjunctivitis with acute inflammation and edema of both palpebral and bulbar conjunctivae and marked chemosis. Moderate photophobia and blepharospasm as well as increased lacrimation were noted. The remainder of the eye examination including funduscopy was not remarkable. Small preauricular nodes were palpable bilaterally. The results of examination of both ears and nose were normal. There were no mouth lesions. The tonsils were hypertrophied and slightly injected. The neck was supple, and the trachea was in the midline. There was a mild generalized lymphadenopathy. The heart was not enlarged on percussion; the rhythm was regular and the rate was not rapid. There were no thrills or shocks. The heart sounds were of good quality. At the apex and along the left sternal border extending to the pulmonic area a blowing, soft systolic murmur was heard. This was not transmitted to the axilla, and was not audible over the neck vessels, back, or to the right of the sternum. The second pulmonic sound was louder than the second aortic sound, but was not accentuated. The pulses were equal, synchronous, regular, and of good quality. The lungs were clear to percussion and auscultation. The abdomen was scaphoid; there was no tenderness nor spasm. The liver, spleen, and kidneys were not palpable. Examination of the extremities was normal except for the right knee, which was swollen, warm, and held in a position of slight flexion. There was spontaneous pain and moderately severe tenderness on palpation. Motion was painful and resisted. There was a moderate effusion into the joint, so that a patellar click was readily demonstrable. The genitalia were those of a normal 4-year-old boy, but the urethral os was slightly crusted. The neurological examination was not remarkable. The skin was slightly pallid, but no unusual lesions were noted.

Course.—The patient's temperature, which shortly after admission rose to 103° F., gradually fell to normal by the end of the third week (Fig. 1).

Warm, wet saline compresses were applied to the right knee, which was elevated on pillows. On the third hospital day the knee joint was aspirated for diagnostic purposes. Approximately 10 ml. of thick, turbid, odorless, yellow-green pus were withdrawn, and 100,000 units of penicillin in 5 ml. of normal saline were injected directly into the joint cavity. The pus, which contained 17,000 leucocytes per cubic millimeter, all polymorphonuclear, was studied for possible bacterial and viral content. From the third hospital day the patient ceased to complain of spontaneous pain in the right knee, although tenderness on pressure persisted. On the sixth hospital day, at the advice of an orthopedic consultant, 4 pounds of traction were applied to the right lower extremity by means of a Buck extension to correct a tendency toward flexion contracture of the knee. As shown in Fig. 1, the subsequent course of the arthritis was one of progressive improvement, so that at the time of discharge, forty-four days after the onset of arthritis, only minimal residual effusion remained with no evidence of deformity or limitation of motion. One month later minimal effusion was still apparent, but two months after discharge, the right knee was entirely normal on clinical examination. Several x-ray studies failed to reveal more than soft tissue swelling with increase in the joint space; no bony abnormalities were found.

The dysuria, frequency, and pyuria subsided at the end of the first week of hospitalization. On the third hospital day some urethral pus and a small amount of prostatic fluid were obtained for study for possible bacterial or viral content.

There was slow but progressive improvement in the condition of the eyes until the eighth hospital day, when an exacerbation of the bilateral purulent conjunctivitis was observed (see Fig. 1). On the following day, the temperature rose to 101° F., and the conjunctival reaction was more marked. In addition, there was noted for the first time some corneal involvement of the right eye. The child was then treated with sulfathiazole ophthalmic ointment, drops of 1 per cent atropine sulfate, warm saline compresses, and injections of boiled milk. After the second week of hospitalization, definite improvement was again noted. The conjunctival reaction diminished, the corneal infiltrates were smaller, and the blepharospasm and photophobia were less apparent. At the time of discharge, thirty-three days after the onset of keratitis, the only residual defect was a small, faint, peripheral opacity of the right cornea; the left cornea had cleared entirely.

At no time during the patient's course in the hospital or during the subsequent months of observation did he exhibit recurrence of the diarrhea noted at the onset of the illness.

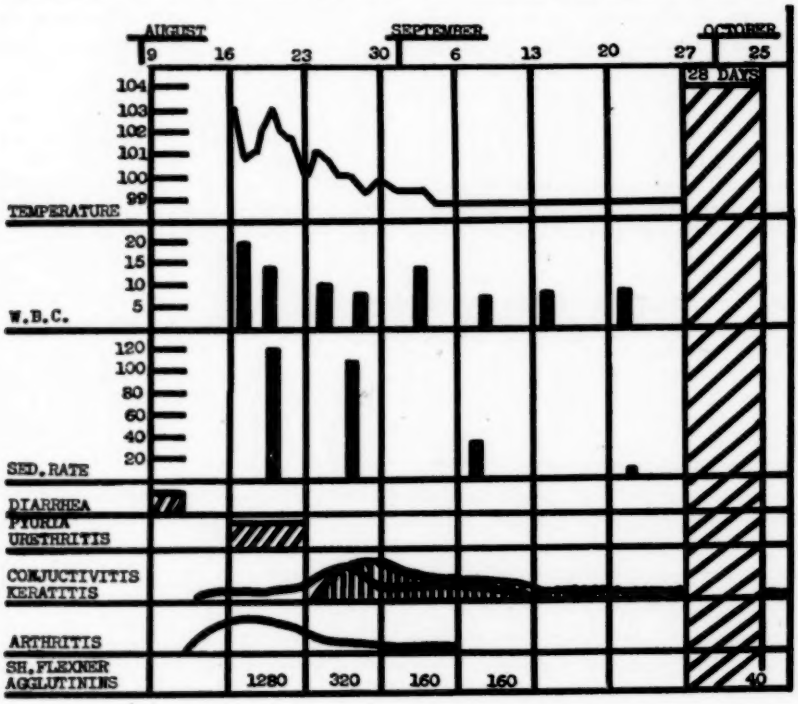

Fig. 1.—Summary of clinical course of patient.

Upon admission, the hemoglobin was 12 Gm., and there was a white blood cell count of 20,050 per cubic millimeter with 79 per cent polymorphonuclear cells. Subsequent blood counts were essentially normal as is graphically recorded in Fig. 1. The sedimentation rate was 120 mm. per hour (Westergren) on admission. It remained quite rapid during the first three weeks in the hospital and did not reach normal levels until the sixth week.

Tuberculin reactions (Mantoux) were negative up to one milligram. The Schick test was negative. Blood urea nitrogen, total protein, and albumin-globulin partition were within normal limits. Repeated tests were made for the development of agglutinins to enteric and other bacteria and are reported below.

During the first ten days of hospitalization the patient was given a course of penicillin therapy in divided doses of aqueous solution every three hours intramuscularly, and penicillin

ophthalmic ointment locally. It is noteworthy that the onset of keratitis occurred during this period of therapy. Subsequently, the already described eye care was given, and sulfadiazine was also given by mouth in dosage of 0.12 Gm. per kilogram of body weight daily for nine days. Despite the progressive clinical improvement noted during this period, it cannot be stated that sulfadiazine exerted any influence on the course of the disease.

Six weeks following discharge the child was readmitted because of a mild conjunctivitis associated with an upper respiratory infection. He was afebrile, and the white blood count and sedimentation rates were normal. There were no urinary symptoms nor urethral discharge. The urine was clear. Conjunctival smear and culture were also negative. There was no diarrhea. Stool culture revealed no pathogen. The joints including the right knee were normal.

When seen four months after the onset of the illness, the only residual abnormality was a minute peripheral opacity of the right cornea, which did not interfere with the child's vision.

BACTERIOLOGY

Material from the conjunctivae and from the affected knee joint obtained shortly after admission was inoculated onto blood agar and chocolate agar plates and into 20 per cent serum broth tubes, which were incubated aerobically and under increased carbon dioxide tension for two weeks. The only organisms recovered were a *Staphylococcus albus* from the conjunctivae and a chromogenic bacillus from the knee fluid. Neither was thought to be significant. Smears of prostatic fluid were stained by Gram's technique, but no organism could be demonstrated. Despite the history of recent diarrhea, only *Escherichia coli communis* was recovered from stool cultures taken the day after admission in tetrathionate broth and on S S, Endo, blood, and nutrient agar plates. Blood cultures also taken on admission in meat extract, glucose, and nutrient broth flasks and liver tubes were negative after two weeks of observation.

VIROLOGY

Rabbit corneas were scarified and inoculated with some of the urethral discharge and knee fluid. The specimens were obtained on Aug. 18, 1947, and stored in lusteroid tubes at approximately 20° C. until satisfactory animals became available. On Sept. 4, 1947, two full-grown rabbits were inoculated with each specimen, and on Sept. 11, 1947, this experiment was repeated using young rabbits, each weighing approximately one kilogram. Although these animals were observed daily for two weeks, no abnormalities were noted. A group of five Swiss mice were also given 0.03 ml. intracerebrally and 0.1 ml. intraperitoneally of the fluid obtained from the patient's knee. They, too, failed to develop any abnormalities during a two-week observation period.

IMMUNOLOGY

Gonococcus complement fixation tests, using the Lederle antigen, were negative with sera obtained Aug. 18 and Sept. 15, 1947. Agglutination tests with serial specimens of serum collected during a three-month period against a pleuropneumonia-like organism which had been recovered from a patient with subacute bacterial endocarditis[9] were carried out for us by Herschberger. These results were also negative. Similarly, agglutination tests were negative for the

development of antibodies for *Eberthella typhi, Salmonella, Brucella,* and *Proteus OX-19* bacteria. However, antibodies in high titer were found for *Shigella flexner VII* and *VIII*. No similar levels were detected for the other Flexner strains. As is indicated in Fig. 1, the results of the child's agglutination tests for *S. flexner VII* fell from a level of 1:1,280 shortly after admission to 1:40 several weeks later. Although this trend was true in many repeated tests, the charted results were obtained with an antigen prepared from an overnight culture on nutrient agar, which was washed three times and killed with 0.5 per cent formalin. From a heavy "stock" suspension, an antigen approximately the turbidity of a MacFarlane No. 3 standard was prepared immediately before use. Serial dilutions of serum were made in 0.4 c.c. quantities of saline. To each an equal quantity of antigen was added. The tubes were shaken, incubated in a 56° C. water bath for one hour, and left at 4° C. overnight before reading. All readings were made by one of us with the aid of a magnifying glass. The highest dilution yielding a 2-plus agglutination (plus 4 = complete agglutination; 0 = no agglutination) was considered the end point.

DISCUSSION

The clinical picture presented by this child was that of an infection. Although it is well known that the triad of arthritis, conjunctivitis, and urethritis can be produced by the gonococcus, it was felt that gonorrhea was excluded in this instance both by culture and by serologic tests.

The failure to recover a virus from this patient does not exclude the possibility that a virus was the etiological agent of the illness. The storage of specimens before inoculation of the rabbits and mice was not ideal. However, according to Buddingh,[10] the virus recovered by him[7] on the rabbit cornea from a patient with Reiter's syndrome would have survived this storage. Because that virus is said to cross immunologically with the one recovered by Buddingh and Dodd[11] from newborn infants with epidemic diarrhea, it is unfortunate that it has not yet been possible to test our patient's serum for neutralizing antibodies against either of these agents.

No pleuropneumonia organisms were recovered. However, search was limited to culture of urethral discharge and knee fluid in serum broth and on chocolate agar. The negative results of the agglutination test with the pleuropneumonia organism of Herschberger and her associates[9] are also of limited significance inasmuch as the degree of immunologic crossing among the various pleuropneumonia strains is not yet known.

The high titer of *S. flexner VII* agglutinins observed in this child's blood ten days after onset of the diarrhea and the subsequent progressive decline would suggest that the diarrhea had been caused by this or a related shigella, despite the recent work by Watt and DeCapito,[12] which shows the unreliability in adults of the agglutination test in such infections. Failure to recover this organism from the stool approximately one week after cessation of diarrhea is not unusual.

It is of considerable interest that in the original as well as in a great many of the other reported cases of this syndrome there was a preceding history of

diarrhea. This fact has been recently emphasized by Young and McEwen.[6] It is also known that arthritis may be a complication of bacillary dysentery and that it frequently appears after the acute symptoms have subsided. The fluid from the joints in such arthritis is usually sterile.[13] Conjunctivitis and iridocyclitis are also recognized complications of dysentery infections.[14]

Study of a single case does not permit an answer to the question of whether this syndrome represents a specific entity or is a nonspecific response of certain individuals to a variety of infections—perhaps an "allergic" response. However, the fact that Reiter's triad of symptoms occurred in a 4-year-old child is significant, especially since the syndrome would seem to be very uncommon in this age group, one in which diarrhea is not infrequent.

SUMMARY

The case history is presented of a 4-year-old boy who, following a short period of diarrhea, developed arthritis, conjunctivitis, and urethritis. Recovery from this syndrome, which was originally described by Reiter, was accompanied by a gradual decline in *S. flexner* agglutinins from a level of 1:1,280 to 1:40. The significance of this observation is not clear. Attempts to recover a pathogenic microorganism, pleuropneumonia-like organism, or a virus from the joint fluids, urethral discharge, and conjunctival smears were unsuccessful.

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PARA-AMINOBENZOIC ACID BLOOD LEVELS

R. D. Lomas, M.D., and G. W. Salmon, M.D.,
With the Technical Assistance of Le Roy Anderson
Houston, Texas

THE clinical value of para-aminobenzoic acid in the treatment of rickettsial diseases has been well established, not only in adults, but also in children. It is our purpose to present the results of a study on the absorption and urinary excretion of para-aminobenzoic acid administered orally, subcutaneously, and intravenously. It is not our aim to formulate a dosage schedule, but only to show the blood levels which may be obtained with different dosages.

METHODS

Our observations were made upon infants and children on the pediatric ward. No adult subjects were used. None of the patients had a rickettsial disease. The subjects were not restricted in any way during the study, being allowed to consume *ad libitum* and to take their meals.

All blood samples were collected in test tubes containing sodium citrate crystals so that no dilution would occur. Para-aminobenzoic acid levels were determined on whole venous blood by a modified Bratton-Marshall method as described by Kirch and Bergeim[1] and Eckert.[2] The free form of para-aminobenzoic acid was always determined, and the conjugated form when it was felt that this would add to our study. All blood level determinations were performed by the same person (L. A.).

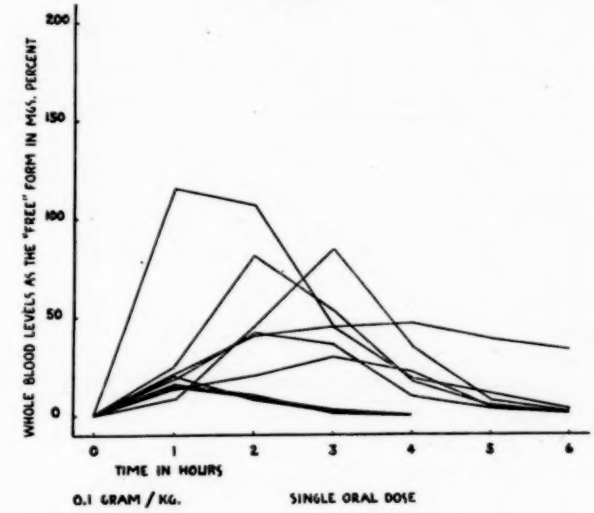
OBSERVATIONS

Para-aminobenzoic acid was administered orally as the sodium salt in the form of tablets (0.25 Gm. and 0.5 Gm.) and, in three cases, as a suspension containing 5.0 Gm. in 30.0 c.c. At no time was para-aminobenzoic acid given by gavage. When a single oral dose (0.1 Gm. per kilogram of body weight) was given, the blood level rose rapidly, in most cases reaching its maximum in the first two hours, and then gradually fell, until only a trace remained at the end of six hours (Fig. 1). The variance in the values and in the rapidity of attaining the maximum levels cannot be explained by differences in the size of the subjects, as their weights ranged from 20 to 25 kg. We are not able to comment upon the ability of the gastrointestinal tract to absorb para-aminobenzoic acid, as no fecal excretion studies were performed. One might surmise, however, from the high percentage excreted in the urine (Fig. 11) that the absorption is fairly complete. When oral doses of 0.2 Gm. per kilogram of body weight were given, the maximum blood levels, as would be expected, were higher (one and one-half times) and more prolonged than with the smaller doses. At

From the Department of Pediatrics, Baylor University College of Medicine, the Hermann Hospital, and the Junior League Children's Clinic, Houston.

the end of the six-hour period the levels were some twenty-five to 100 times as great (Fig. 2). The rapidity of the fall of the blood levels in all of these studies was influenced by the liquid intake of the individual, as this was not restricted.

Fig. 1.



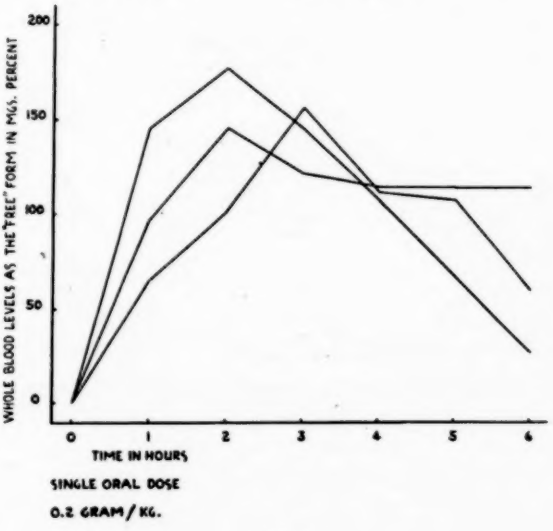
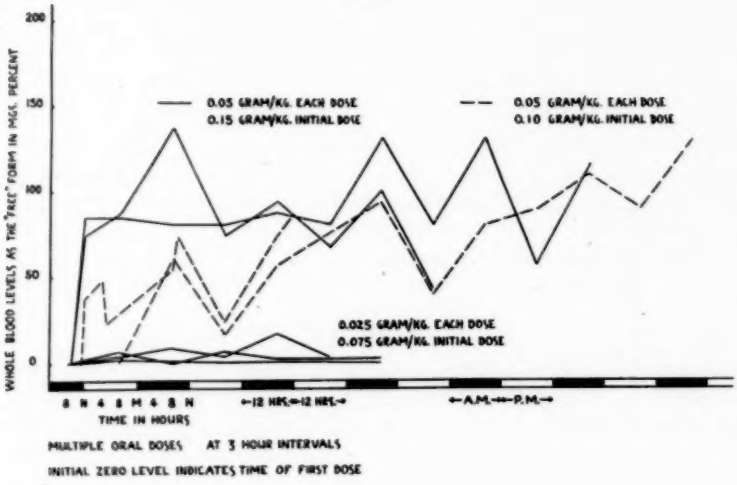


Fig. 2.

Our studies on multiple oral doses are summarized in Figs. 3 and 4. It is apparent that 0.025 Gm. per kilogram of body weight at three-hour intervals does not maintain significant levels. Twice this amount, however, maintained

Fig. 3.


WHOLE BLOOD LEVELS AS THE "FREE" FORM IN MGS. PERCENT
200
150
100
50
0
0.05 GRAM/KG. EACH DOSE
0.15 GRAM/KG. INITIAL DOSE
0.05 GRAM/KG. EACH DOSE
0.10 GRAM/KG. INITIAL DOSE
0.025 GRAM/KG. EACH DOSE
0.075 GRAM/KG. INITIAL DOSE
8 N 4 8 M 4 8 N
←12 HRS.→←12 HRS.→
←A.M.→←P.M.→
TIME IN HOURS
MULTIPLE ORAL DOSES AT 3 HOUR INTERVALS
INITIAL ZERO LEVEL INDICATES TIME OF FIRST DOSE

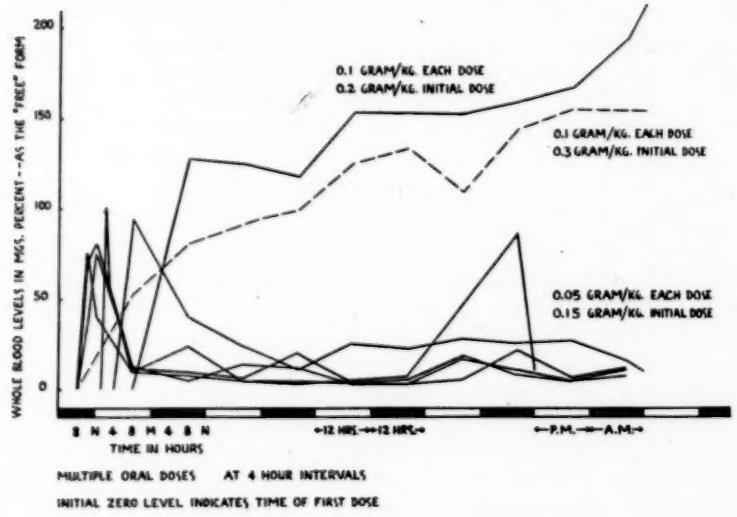
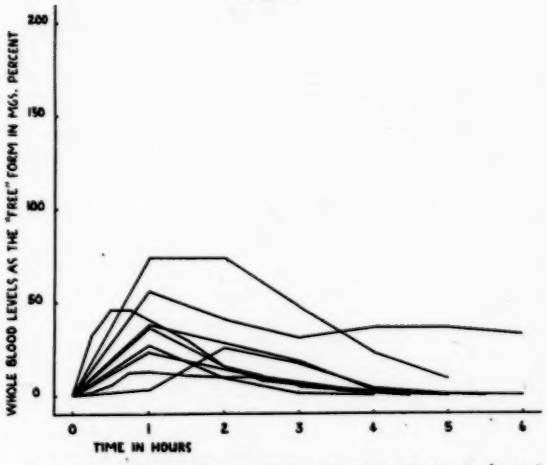

WHOLE BLOOD LEVELS IN MGS. PERCENT--AS THE "FREE" FORM
200
150
100
50
0
0.1 GRAM/KG. EACH DOSE
0.2 GRAM/KG. INITIAL DOSE
0.1 GRAM/KG. EACH DOSE
0.3 GRAM/KG. INITIAL DOSE
0.05 GRAM/KG. EACH DOSE
0.15 GRAM/KG. INITIAL DOSE
8 N 4 8 M 4 8 N
←12 HRS.→←12 HRS.→
←P.M.→←A.M.→
TIME IN HOURS
MULTIPLE ORAL DOSES AT 4 HOUR INTERVALS
INITIAL ZERO LEVEL INDICATES TIME OF FIRST DOSE

Fig. 4.

Fig. 5


WHOLE BLOOD LEVELS AS THE "FREE" FORM IN MGS. PERCENT
200
150
100
50
0
0
1
2
3
4
5
6
TIME IN HOURS
SINGLE SUBCUTANEOUS DOSE OF SODIUM SALT IN NORMAL SALINE (1% SOL.)
0.1 GRAM / KG.

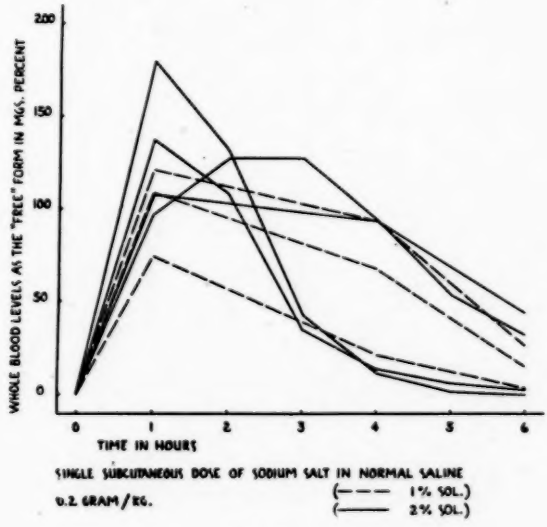
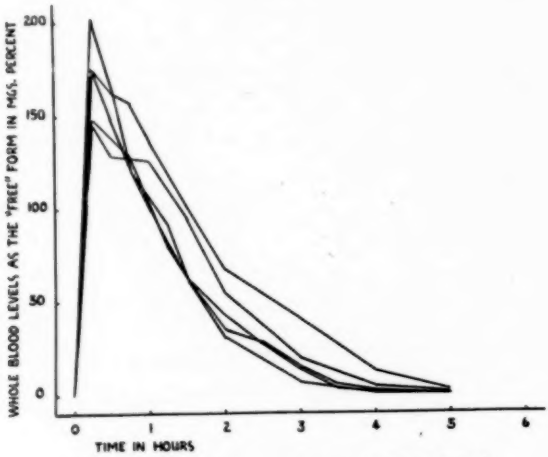

WHOLE BLOOD LEVELS AS THE "FREE" FORM IN MGS. PERCENT
200
150
100
50
0
0
1
2
3
4
5
6
TIME IN HOURS
SINGLE SUBCUTANEOUS DOSE OF SODIUM SALT IN NORMAL SALINE
0.2 GRAM / KG.
(– – – 1% SOL.)
(——— 2% SOL.)

Fig. 6

levels averaging 75 to 100 mg. per cent. This same amount (0.05 Gm. per kilogram) at four-hour intervals did not maintain significant levels. At this same time interval (four-hour) 0.1 Gm. per kilogram of body weight produced ex-

Fig. 7.



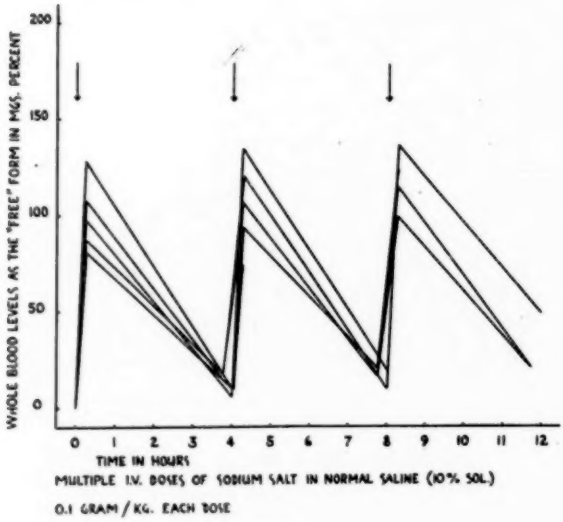


Fig. 8.

ceedingly high levels. It is of interest that these figures show that the early morning levels were always higher than at other times of the day; this was probably due to voluntary restriction of liquids during the sleeping hours.

Para-aminobenzoic acid in the form of its sodium salt may be administered parenterally. The need for parenteral therapy has been emphasized by Ravenel.[3] The drug may be administered either subcutaneously or intravenously. The maximum levels obtained by subcutaneous injection (0.1 Gm. per kilogram of body weight as a one per cent solution in normal saline) were not as great as when the drug was given orally, but were attained more rapidly (Fig. 5). The blood levels were increased when the dose was doubled (0.2 Gm. per kilogram of body weight) (Fig. 6). Moreover, when this same dose was given in a 2 per cent solution, the blood levels were further increased. There were no reactions when this drug was administered subcutaneously in solutions as strong as 3 per cent in normal saline.

An immediate blood level rise to over 150 mg. per cent was obtained after giving sodium para-aminobenzoic acid intravenously (0.1 Gm. per kilogram of body weight as a 10 per cent solution in normal saline). Following this, the level rapidly declined (Fig. 7). Multiple intravenous injections given at four-hour intervals failed to produce a sustained blood level (Fig. 8).

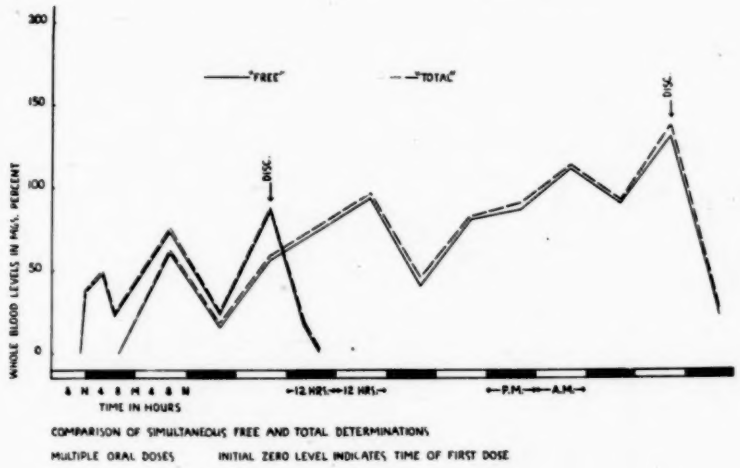
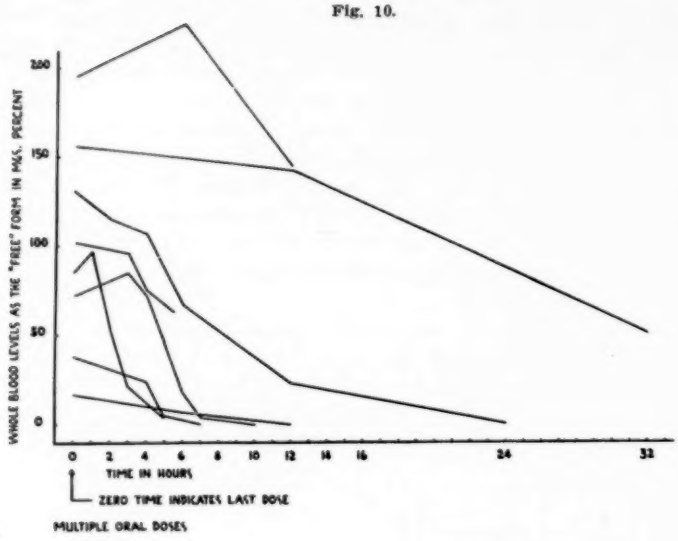


Fig. 9.

Values for total para-aminobenzoic acid were slightly higher than for the free form. The two values paralleled each other throughout (Fig. 9). The difference between the levels is accounted for by the conjugation (acetylation) of a small portion of the drug within the body. It is worthy of note that the percentage of the conjugated form did not increase when the drug was given over a period of several days.

It will be noted that following administration of a single dose by any route used in this study, the drug has largely disappeared from the blood in about six hours. The rapidity of the disappearance seems to be inversely related to the height of the blood level obtained. When the drug was discontinued fol-

Fig. 10.



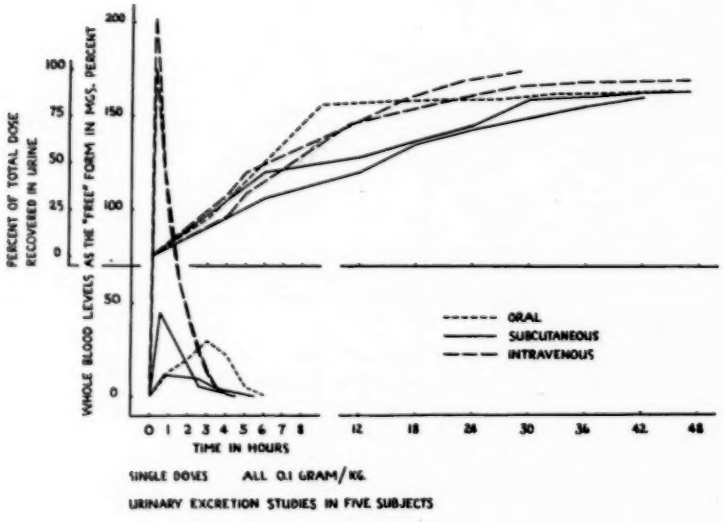


Fig. 11.

lowing multiple oral doses (Fig. 10), it possibly persisted in the blood for a somewhat longer period of time. These results may be suggestive of storage of para-aminobenzoic acid within the body for at least a short period of time. Moreover, the results shown in Fig. 11 demonstrate that, following a single dose, urinary excretion is continued for more than twenty-four hours after the drug has disappeared from the blood.

Each subject receiving para-aminobenzoic acid was followed with hemograms and urinalyses. No abnormalities were noted. Vomiting was minimal.

CONCLUSIONS

Para-aminobenzoic acid is rapidly absorbed from the gastrointestinal tract. An adequate blood level is maintained in most instances when one-half or one-third the initial dose is given as a maintenance dose every three hours. Subcutaneous administration of solutions as strong as 3 per cent were without ill effects. The rapidly rising blood levels and the maintenance of these levels over a period longer than six hours makes this method of administration feasible and useful. Intravenous administration of the drug produced high levels rapidly, but these were not maintained. The prolonged excretion of the drug in the urine is suggestive of storage within the body.

We wish to express our appreciation to Dr. Edwin E. Garrett for his aid in this study.

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INCIDENCE OF SICKLE CELL ANEMIA WITH RHEUMATIC HEART DISEASE

IRVING ROBERT OHRENSTEIN, M.D.*
PHILADELPHIA, PA.

THE confusing resemblance between the symptoms of sickle cell anemia and those of rheumatic heart disease is well known. Yater and Hansmann[1] have pointed out that the diagnosis of rheumatic heart disease in cases of sickle cell anemia has been made many times from the history of joint pains, presence of an enlarged heart, systolic mitral or precordial murmur, and hepatomegaly. Other common symptoms are leg pain, ankle edema, pallor, and dyspnea. Oftentimes organic heart disease is diagnosed clinically only to find at autopsy that all changes noted are compatible with a severe anemia.

That anemia is a cause of heart disese has often been overlooked. In accordance with the Criteria Committee of the New York Heart Association, the criteria are as follows: (1) presence of a marked anemia, (2) disturbance of cardiac function, (3) disappearance of signs and symptoms after relief of the anemia.

Sickle cell anemia is hereditary and is somewhat refractory to treatment. It is characterized by exacerbations and remissions, and therefore the third criterion cannot be satisfactorily met except for relatively short periods of time. Over a period of years, the anoxia secondary to the anemia gives rise to alternating severe strains upon the heart. This relationship of cause and effect between the anemia and cardiac abnormalities cannot be overlooked nor can it be denied.

In 1932 Anderson and Ware[2] reviewed the literature and found cardiac enlargements in 76 per cent and murmurs in 87 per cent of those cases in which mention was made of the presence or absence of these findings. Klinefelter[3] has shown that the clinical findings in sickle cell anemia could closely simulate those of rheumatic heart disease, but noted that specific lesions have never been demonstrated at autopsy. Hansman emphasized the importance of being extremely cautious in making a nonanemia diagnosis of heart disease when studying a patient with sickle cell anemia. The clinical discussion as to whether sickle cell anemia alone is present or whether there is an accompanying rheumatic heart lesion is made even more complex by Cooley's[4] statement: "Organic heart disease is about as common here (sicklemia) as in any group of children subject to tonsillitis as these children often are."

In an attempt to clarify the confusion, the pathology files of the Cook County Hospital were searched in order to ascertain the incidence of sickle cell anemia concomitant with rheumatic heart disease. Since 1929, fifty-three autopsies have been performed on individuals who gave positive evidence of sickle cell anemia. In thirteen cases, or 24 per cent, the sickle cell anemia was

*Formerly Pediatric Resident, Cook County Children's Hospital, Chicago.

the direct cause of death. Of this group, ten patients were below 3 years of age. In forty cases, or 76 per cent, the sickle cell anemia contributed indirectly to the cause of death. Of this group, four patients were below 3 years of age. Three patients showed evidence of rheumatic heart disease, and the primary anatomic diagnosis in two of these was rheumatic heart disease. The ages of these three patients were 3, 7, and 22 years. The incidence of sickle cell anemia concomitant with rheumatic heart disease was 5.6 per cent.

CASE REPORTS

CASE 1.—Negro girl, aged 22. Several months prior to the present admission the patient had been in this hospital. At that time she gave a typical history of rheumatic heart disease with cardiac involvement since childhood; her complaints were severe dyspnea, orthopnea, constant precordial pain, and some peripheral edema. It was also found that she had an active case of sickle cell anemia. She remained in the hospital for eight weeks and was discharged. At the time of the second admission, which was twelve weeks after her previous discharge, her complaints again were precordial pain, weakness, nodules in the calves, cough, and slight hemoptysis.

Physical Examination.—The temperature was 99.6° F., pulse 112, respirations 24, blood pressure 90/50. There was marked pallor of the conjunctivae, the heart was enlarged to the left with a loud systolic and presystolic murmur; the rhythm was regular, the tones distant, P_2 accentuated. The liver was felt below the level of the umbilicus. There was slightly diminished resonance in the lower lobe of the right lung.

Laboratory Findings.—On x-ray the heart showed a mitral configuration. The hemoglobin was 9.5 Gm., the red blood count 3.65 million, the white blood count 10,150. There was marked sickling. The urine was negative except for 3 plus albumin on one occasion.

Further Course.—The patient remained in the hospital until her death six weeks after admission. During her hospital stay she was given repeated blood transfusions and put on a regular cardiac regimen. There was, however, no relief of her symptoms, and she gradually became worse and died.

Autopsy Report.—The body was that of a well-developed, well-nourished Negro girl, who showed no external pathologic findings; there was no edema of the ankles.

Heart: The heart weighed 550 Gm. The wall of the left ventricle measured 18 mm. in thickness and that of the right ventricle, 5 mm. The myocardium was pale purple-red; there were numerous fibrous tags attached to the epicardium with many pinhead-size subepicardial hemorrhages. The free edge of the mitral valve revealed many pinhead-size single and confluent light yellow-gray, soft elevated nodules. These were also present in the endocardium along the left auricle near the mitral valve. All chambers were dilated markedly and the endocardium of both auricles and of the interventricular septum was gray-white and thickened. The papillary muscles were hypertrophied. There were numerous fibrous adhesions of the pericardial sac to the epicardium. Both coronary arteries were thickened markedly; there were many atheromatous plaques, but the lumen was patent throughout. The pulmonic valve measured 76 mm. There was a single fatty and hyaline plaque.

Spleen: The spleen weighed 140 Gm. It was very firm, and the capsule was slightly thickened and smooth. On section, dark purple-red trabeculae were prominent. The lower pole was located at the ninth rib in the midaxillary line.

Liver: The liver extended 12 cm. below the xiphoid process and 3 cm. below the costal margin. It weighed 2,000 Gm., was very soft and flabby, and the capsule was thickened. There were many adhesions attached to the capsule of the right lobe. On section, deep red-purple and acinar centers were confluent, leaving small islands of light yellow peripheral acinar markings.

Bone marrow: The bone marrow was cherry red.

Microscopic examination.—

Heart: The muscle fibers were swollen and hypertrophied; the nuclei were oval to barrel-shape; the cytoplasm was pale pink and granular. Cross-striations were indistinct. There was

an increase of interstitial fibrous connective tissue, more marked around the large vessels. The epicardium was edematous and thickened with round cell infiltration. The capillaries were dilated. The fat stain showed slight deposition of fat in muscle fibers.

Liver: The architecture was destroyed. There were remnants of liver cell cords around the portal triad and near the capsule, which were swollen, purplish pink, and had granular cytoplasm. Sinusoids of these cells were moderately compressed and contained red blood cells, and a few round cells. Kupffer cells were prominent and numerous. The remainder of the liver cell cords were intact and showed normal liver cells. There was a deposit of hemosiderin pigment granules in the macrophages throughout the entire section. The portal triad showed slight proliferation of bile ducts. Sudan iii stain revealed a deposition of sudanophilic droplets in the remaining cords. The red blood cells were thin and sickle-shaped.

Spleen: The capsule was of normal thickness. The sinusoids were enormously congested with red blood cells, which were thin and sickle-shaped. There were many polymorphonuclear leucocytes scattered throughout. The lymphoid tissue was sparse and most of it was around the central arteries. Here and there were hyalinized, light pink areas, which appeared to contain free hemoglobin. There were many hemosiderin pigment granules throughout.

Bone marrow: There were more centers of erythropoietic activity than normally found. The granulocytic elements were of ordinary distribution. The megakaryocytes were numerous throughout.

CASE 2.—Negro boy, aged 7. The patient was well until three days prior to admission when he developed abdominal pain. This lasted one hour, and then he developed pain in the left groin and leg. This was transient; the pain was next felt in the head and shoulders, only to return to the stomach two days later, when he vomited once. There was nocturia with the voiding of reddish urine one to three times each night. His past history revealed that he had had several attacks of typical rheumatic fever, beginning at one year of age, and swelling of the feet at 4 years of age.

Physical Examination.—The patient was undernourished. There were markedly hypertrophied postauricular nodes, mild axillary lymphadenopathy, markedly enlarged bilateral inguinal nodes, and slightly tender epitrochlear and posterior popliteal lymph nodes. The lungs were negative. The pulse was 140 per minute. There were blowing systolic and diastolic murmurs. The liver was felt one fingerbreadth below the costal margin and was slightly tender. The temperature was 102° F. The patient had long tapering fingers.

Laboratory Findings.—On x-ray, the heart was enlarged in its transverse diameter and had a contour of mitral type. The hilar and perivascular markings were increased, suggesting some passive congestion.

The red blood count was 2.14 million, the white blood count 25,000, with 69 per cent polymorphonuclear leucocytes, metamyelocytes, 7, and lymphocytes, 24. A blood smear showed positive sickling, polychromatophilia, and anisocytosis. The urine was negative. The icterus index was 15.

An electrocardiogram suggested pathologic change in the right heart.

Course and Treatment.—By the second hospital day the temperature was 104.2° F. There was tenderness in the right upper quadrant and increased soreness in the abdomen, which was rigid to palpation. Pulse was 140, respirations, 22 to 30. The patient was given plasma and 5 per cent glucose. He developed a gallop rhythm and failing heart. After sickling was demonstrated, the patient was given transfusions. The temperature remained elevated at 105.8° F. rectally. He was placed on 5 per cent glucose because of the liver damage and given continuous oxygen. By the fifth day a precordial friction rub was heard, the liver was increased in size, and the patient remained markedly restless and dyspneic. He expired on the sixth hospital day.

Autopsy Findings.—The essential autopsy findings were as follows:

Heart: The heart weighed 253 Gm. The myocardium was medium red in color and of medium firmness. The wall of the left ventricle measured 15 mm. in thickness, of the right ventricle, 3 mm. The pulmonary valve measured 55 mm. The aorta measured 55 mm. The intima was light yellow in color and smooth. There were small verrucous vegetations along

the line of closure of the mitral valve cusps. The mitral valves were fibrous and somewhat contracted, and the papillary muscles were markedly shortened, thin, and fibrous. The left ventricle was extremely dilated. There was a bread and butter type of fibrinous pericarditis of the pericardial sac, which was fairly easily separated.

Spleen: The spleen weighed 111 grams; the consistency was very firm, the capsule light gray and smooth. On section, the spleen was deep red in color. The follicles were fairly prominent.

Liver: The liver weighed 1,215 Gm. The consistency was firm; the capsule was smooth and glistening. On section, it was medium yellowish red in color.

Microscopic examination.—

Heart: In some of the fibrinous septa, there were aggregations of round cells, suggestive of an old rheumatic process. The red blood cells in the blood vessels showed sickling.

Bone: There were a large number of nucleated red blood cells.

CASE 3.—Negro girl, aged 3 years. Patient entered with complaints of fever for five days, rash five days, and dyspnea and profuse nasal discharge for three days.

Physical Examination.—The temperature was 104° F., pulse 160, respirations 40. The conjunctivae were injected; there was profuse, green, sanguineous nasal discharge. The pharynx was inflamed, and there was a mucoid discharge. The tonsils were hypertrophic and inflamed. The lungs were clear with slight retractions on inspiration in all interspaces. The heart was normal.

Laboratory Findings.—No urinalysis or blood count was reported. A smear of the nasal discharge showed short chain streptococci.

Course.—The patient ran a downhill course and expired two days after admission.

Autopsy Findings.—

Heart: The heart weighed 55 Gm.; both ventricles were dilated; the epicardium and endocardium were delicate; the myocardium was firm and bluish red.

Spleen: The spleen weighed 95 Gm. and measured 13 by 7 by 4 cm. It was large, dark bluish red, and stony hard. On cut section, the spleen was smooth and the follicles small.

Liver: The liver weighed 575 Gm. and was of normal size and configuration. On cut section it showed only slight congestion.

Microscopic findings.—

Heart: The capillaries were congested. There were many Aschoff nodules around the small arteries, consisting of round cells, Anitschkow's cells, and plasma cells.

Spleen: The sinusoids were dilated and crowded with sickle-shaped red blood cells.

Liver: There were focal areas of congestion.

Red blood cells in all organs showed sickling.

SUMMARY

An attempt has been made to ascertain the incidence of sickle-cell anemia concomitant with rheumatic heart disease. Fifty-three autopsies have been performed at Cook County Hospital since 1929 on individuals who gave positive evidence of sickle-cell anemia. Of this group there were three patients who showed concomitant findings of rheumatic heart disease. The incidence was 5.6 per cent.

I wish to thank Dr. I. Pat Bronstein, Associate Professor, Department of Pediatrics, University of Illinois College of Medicine, for his interesting discussion, which stimulated this investigation.

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ERYTHROBLASTOSIS FETALIS ASSOCIATED WITH Rh-POSITIVE MOTHERS

CHARLES CHESNER, M.D., AND JOSEPH A. CICERRELLA, M.D.
LORAIN, OHIO

FOLLOWING close upon Landsteiner and Wiener's[1] discovery of the Rh factor, Levine and his associates[2] developed the idea of maternal isoimmunization in the pathogenesis of erythroblastosis fetalis, demonstrating the relationship between Rh incompatibility and erythroblastosis fetalis. In over 90 per cent of the cases the father and child were Rh positive and the mother, Rh negative. Clinically, erythroblastosis fetalis is considered as a single disease with three chief recognized forms, called fetal hydrops, icterus gravis, and congenital anemia.

Erythroblastosis fetalis is generally considered as being synonymous with Rh incompatibility and associated with Rh-negative mothers in over 90 per cent of the cases. However, not all cases of erythroblastosis fetalis are caused by the Rh antigen-antibody reaction. On a theoretical basis, incompatibilities can occur from any blood antigen which is present in the father, transmitted to the offspring, and absent in the mother. The Rh subgroups, the Hr factor, and ABO group incompatibilities are possible etiological agents. The M, N, and P factors are apparently not antigenic. Tovey[3] gives four reasons why the fetus enjoys protection from the mother's agglutinins in heterospecific pregnancies:

1. There is lack of placental permeability to anti-A or anti-B agglutinins.
2. Fetal plasma neutralizes the A or B antibodies.
3. Fetal erythrocytes are not sufficiently sensitive.
4. The A and B antibodies do not react very well at body temperature.

We are presenting two cases because they were both diagnosed clinically as erythroblastosis fetalis and in both the mothers were Rh positive. Likewise, in both cases the paternal and maternal bloods were identical in Rh groupings, subgroupings, and Rh factor, with the absence of Rh antibodies from the maternal blood.

One infant was diagnosed as having congenital hydrops and died about one-half hour after birth. The Rh, Hr, and ABO groupings of both parents were identical. Antibodies were absent from the maternal blood. We believe that this can be classified as a case of universal edema of the fetus unassociated with erythroblastosis as described by Potter[4] The second patient showed jaundice, anemia, and erythroblastosis with no incompatibilities of the Rh or Hr groups. Instead there was an incompatibility of the ABO groups with a high maternal anti-A agglutinin titer.

CASE REPORTS

CASE 1.—The mother was gravida i, para 0; there had been no miscarriages and there was no history of transfusions. The serology was negative. The pregnancy itself was un-

From St. Joseph's Hospital, Lorain, Ohio.

eventful. The child was born after a prolonged second stage. The scalp was edematous and suture lines were not made out. The extremities were tense and rigid. The head appeared attached to the body. The amniotic fluid was bloody. The child lived about forty minutes. The estimated gestation age was about 8 months. A clinical diagnosis of erythroblastosis fetalis, hydrops type, was made.

An autopsy was performed. Marked edema of the entire body was noted, with edema of the rectus muscle. There were blotchy, bluish red spots over the skin surface. The abdomen was filled with a blood-tinged fluid. There were accumulations of a clear fluid in the pleural cavities, with compression of the lungs. The liver weighed 120 Gm. and the spleen, 12 Gm. There was marked hemorrhage into the soft tissue beneath the scalp, which formed a one centimeter membrane over the calvarium. The sections showed extensive extrahematopoiesis in the liver and small interstitial cellular accumulations in the rectus muscle, probably myeloid metaplasia. Other findings were not significant. The final diagnosis was congenital fetal hydrops, not associated with erythroblastosis. There were extrahematopoietic foci in liver (extensive) and muscle (few), edema of body surfaces and subcutaneous tissues, ascites and bilateral hydrothorax, and bilateral atelectasis.

The mother's and father's blood was sent to Dr. Anna May Young of Cleveland and Dr. Mary Lou Scholl of Columbus, Ohio.

The mother's blood was Type A, Rh_0' positive, Hr positive, MN. The father's blood was Type A, Group Rh_0' positive, Hr positive, M. There were no demonstrable antibodies in the mother's blood, and the maternal and paternal bloods were completely compatible. Fetal blood was not available for examination.

The history, serologic findings, and most of the microscopic sections were sent to Dr. Edith L. Potter in Chicago. She agreed that everything fitted into a diagnosis of fetal hydrops without erythroblastosis except the appearance of the liver. She thought that the amount of erythroblastosis in the liver was probably explainable on the basis of fetal age.

CASE 2.—A 23-year-old white woman was admitted to the hospital for her first delivery. The patient had had a normal pregnancy and delivered without difficulty an 8-month male infant with a birth weight of 3 pounds and 12 ounces. The infant had some difficulty in breathing following delivery; respirations were shallow and irregular. The infant's color was pale, and he had a weak cry. He was given alphalobeline, oxygen, Coramine, and vitamin K intramuscularly, and also mouth-to-mouth breathing. Twenty-four hours after birth the child became jaundiced and had rigid extremities, and his condition became critical. He was immediately given 20 to 30 c.c. of the father's blood intramuscularly and one ampule of vitamin K every twelve hours intramuscularly. The respirations became irregular and shallow, and cyanosis developed. A diagnosis of erythroblastosis fetalis was made.

Pediatric consultation was obtained. Physical examination of the baby revealed a critically ill infant, jaundiced, and with very shallow, irregular respirations. The liver and spleen were palpable, and the infant was somewhat dehydrated.

The laboratory report showed that the infant was Type A, Rh positive, with a 52 per cent hemoglobin (Sahli). The mother was Type O, Rh positive. The blood smear of the infant revealed over 100 normoblasts per 100 white cells. The infant was immediately given small Type A Rh-negative blood transfusions intravenously (7 to 10 c.c. per pound of body weight). The baby responded well to the transfusions, and his hemoglobin went from 52 per cent to 104 per cent at one time, reaching a stationary point of 80 per cent at the end of twenty-seven days. Further laboratory work at this time done by Dr. Mary Lou Scholl of Columbus, Ohio, revealed the following:

Mother: O, Rh-positive—Hr positive heterozygous,
Father: A, Rh-positive—Hr negative homozygous,
Baby: A, Rh-positive—Hr positive heterozygous,
Mother: anti-A titer = 1:4,000 (normal 1:64).

The condition of the child remained good until the seventeenth day after birth, at which time the infant started to have frequent bowel movements with mucus and blood. The abdomen became distended and his condition became critical. Surgical consultation entertained the possibility of intussusception, but repeated enemas relieved the condition.

On the forty-second day of life, the infant's hemoglobin dropped to 42 per cent and again Type A Rh-negative blood transfusions were given. Final hemoglobin at time of discharge was 76 per cent.

The child maintained a temperature between 97° and 100° F. throughout his entire stay in the hospital. The baby was followed by the private physician, and the hemoglobin has now been 70 per cent for the past three to four months. The general condition of the child is good, as is his growth and development.

DISCUSSION OF CASES

The diagnosis of fetal hydrops unassociated with erythroblastosis as described by Potter, is supported by the following facts: (1) primiparity of the mother, (2) no history of previous pregnancy or transfusions, (3) Rh-positive mother, (4) absence of antibodies from maternal blood, and (5) identical ABO, Rh, and Hr groupings of mother and father. There was, therefore, no antigenic factor present in the father's blood that was not present in the mother's. The differences in the M and N groups can be discounted as far as antigenicity is concerned. A sixth supporting fact was the compatibility of paternal and maternal blood by direct examination.

The histologic studies left some room for doubt. There was an unusual amount of extrahematopoiesis in the liver, but this probably can be explained on the basis of prematurity. Except for one focus in the rectus muscle (and this was adjacent to an area of hemorrhage), there was no unusual extramedullary hematopoiesis in the other organs.

The etiology of this condition is unknown. A number of cases have been associated with other abnormalities, such as cleft palate and congenital heart disease. The differentiation from true erythroblastosis is important, because the prognosis here as far as future pregnancies are concerned is good.

In our second case, the diagnosis of erythroblastosis unassociated with the Rh factor was supported by the following facts: (1) jaundice and severe anemia in the child, (2) large numbers of erythroblasts and normoblasts in the peripheral blood, (3) presence of large spleen and liver, (4) identical Rh groupings of mother and father, (5) mother was Rh positive, (6) absence of Rh antibodies from maternal blood, (7) father and child were Type A and mother, Type O, and (8) anti-A type of maternal blood was 1:4,000.

GENERAL DISCUSSION

Erythroblastosis associated with an ABO incompatibility was present in nine of 150 infants (6 per cent) seen by Polayes and Ohlbanen[5] and in two of 100 infants seen by Boorman and his associates.[6] All mothers were Rh positive. Most babies were Group A. Group B isoimmunizations were very unusual.

Very rarely both Rh and ABO incompatibilities may exist in the same patient. Wiener and his associates[7] believe that when an Rh-negative woman is exposed to an Rh-positive blood of an incompatible type, the principle of competition of antigens may operate with suppression of the Rh factor.

The mechanism of pathogenesis of erythroblastosis associated with an ABO incompatibility is similar to that when the Rh factor is involved. In the latter,

there is an Rh-positive father and offspring, and an Rh-negative mother. The Rh factor of the fetus acts as a foreign antigen when it gets into the maternal blood stream across the placenta, and sets up an antibody reaction. When the antibodies reach the fetal blood across the placenta, they act on the Rh-positive cells and produce hemolysis. By substituting the Group O mother for the Rh-negative mother, and an A or B fetus for the Rh-positive fetus (or any series of incompatible A, B, O antigens), one can demonstrate the same mechanism.

The surprising feature is not that an ABO incompatibility may lead to erythroblastosis, but that it does not do so more frequently. The factors in the production of erythroblastosis and the protective mechanisms involved are admirably discussed in papers by Boorman and his co-workers,[6] Tovey,[3] Wiener and his associates,[7] Bryce and her associates,[8] and Potter.[9] The main points in the protective theories are as follows:

1. The maternal alpha and beta agglutinins are usually of low titer.
2. The placenta acts as a barrier against these agglutinins, since they are large molecules.
3. There is relative lack of sensitivity of the fetal red blood cells to agglutination. This is probably associated with their incomplete development.
4. Alpha and beta antibodies are absorbed by extracorpuscular group-specific antigens before they get into the fetal blood stream.

Wiener and his associates,[7] Boorman and his co-workers,[6] and Smith,[10] found that the majority of infants producing maternal agglutinins were secretors (normally 80 per cent are secretors and 20 per cent, nonsecretors). Isoimmunization was probably brought about by the passage of the soluble group-specific substances across the placenta.

In view of the hypothetical nature of the factors involved in the possible protective mechanism, it is not at all surprising to find conflicting reports on the relationship between maternal titer and fetal injury.

Polayes and Ohlbanen[5] found that the average anti-A titer of Group O women who had never borne children was 59 (from 20 to 100), and in those who had borne normal Type A children the average was 215 (from 120 to 300). Of the cases of erythroblastosis reported by them, the anti-A titer in maternal blood ranged from 600 to 1,280. Smith[10] recorded a distinct rise in maternal agglutinins in heterospecific pregnancies. In forty out of forty-six pregnancies, there was a rise in titer up to 12,800, with no evidence of harm to the babies. Bryce and her co-workers[8] found a rise of titer in all cases of ABO incompatibilities in which there was damage to the infant. Boorman and his associates[6] found anti-B agglutinins incompatible with the fetal red blood cells with titers of 32,000 and 8 million, in two cases of erythroblastosis. In one normal case there was an anti-A titer of 32,000 or over. In sixteen other normal cases, the anti-A and anti-B titers ranged between 56 and 400. Aubert and his associates[11] reported one case of erythroblastosis proved by autopsy in which the maternal anti-A titer rose to 16 million. In the case reported by Gruber and his co-workers[12] the anti-B titer was 400.

Boorman and his associates[6] made the statement that the maternal titer was not the only important thing. It is the effect on the fetus that counts,

and this depends on the permeability of the placenta, the amount of extracorpuscular group-specific substance, and probably the other protective factors discussed. The titer was probably the important thing with the Rh incompatibility and the amount of extracorpuscular group-specific substances in the ABO incompatibilities.

CONCLUSIONS

1. The clinical diagnosis of erythroblastosis is commonly associated with an Rh incompatibility, occurring in Rh-negative women in over 90 per cent of the cases.

2. Two cases of clinically diagnosed erythroblastosis are presented. In both, the women were Rh-positive with no Rh or Hr incompatibilities.

3. One case was due to an ABO incompatibility.

4. The other case was diagnosed as fetal hydrops unassociated with erythroblastosis fetalis. The diagnosis was established by a thorough serologic study and autopsy. Because of the difference in prognosis as far as future pregnancies are concerned between this and fetal hydrops associated with erythroblastosis, it is important to arrive at a correct diagnosis.

5. A discussion of the immunologic aspect of the ABO incompatibility is presented with reference to the factors involved in the protective mechanism.

We wish to thank Drs. Louis Hait and N. A. Tillman of Lorain, Ohio, for permission to review their cases. We also wish to thank Drs. Mary Lou Scholl of Columbus, Ohio, and Mary Ann Young of Cleveland, Ohio, for performing complete blood examinations and antibody determinations, and Dr. Edith Potter for reviewing the case of fetal hydrops.

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RUPTURE OF LIVER AND SPLEEN IN THE NEWBORN INFANT*

PETER GRUENWALD, M.D.
BROOKLYN, N. Y.

THE present series of cases of rupture of the liver or the spleen, or both, will be reported in order to point out a possible cause of these injuries which, if properly understood, might be avoided in some instances.

Rupture of the liver is not a very rare finding at autopsy in newborn infants. Among those who have reported cases and reviewed the subject, Genell,[1] Lundqvist,[2] Ehrenfest,[3] Rogers,[4] Schmitt,[5] Silver,[6] and Henderson[7] might be mentioned. These and other authors have reported a relatively high incidence of birth trauma to the liver in infants larger than average but have also found it in small, premature infants. This distribution is not surprising and parallels that of cerebral birth injuries. Genell[1] studied the possible mechanisms by which the liver may be injured at birth and assumed that bending and compression of the body are the causes. The former may occur in certain manipulations which are occasionally used in delivery and resuscitation, and result in lacerations extending inward from the surface of the liver. Compression, on the other hand, should produce lesions in the interior of the organ, and Genell suggests that such lesions might be discovered more frequently if the liver of each newborn infant were sectioned carefully at autopsy. McNitt[8] mentions pressure or torsion of the fetal abdomen, including even gentle ante-partum manipulations. Belohradsky[9] implicates severe congestion of the liver in asphyxia as a predisposition to rupture, and this possibility is also acknowledged by Henderson.[7] As an indication of the frequency of birth injury to the liver, Potter's[10] statistical analysis of 2,000 unselected autopsies of newborn and stillborn infants may be mentioned. This series contains twenty-four cases of laceration of the liver. In all instances recorded in the previously mentioned reports, the diagnosis was made at autopsy. To the best of my knowledge, the only cases in which the condition was diagnosed during life and successfully treated are those of Rubovitz[11] and Arden.[12] Rogers[4] suggests abdominal paracentesis for the diagnosis of hemoperitoneum.

Rupture of the spleen is much less common than that of the liver. Lundqvist[2] found it in one case compared with five cases of ruptured liver. In that one infant the liver was large and showed syphilitic changes. Lundqvist quotes Hedren as stating that rupture of the spleen occurs only in syphilitic infants. In a case recorded by Rhamy,[13] the spleen weighed 125 Gm., and the underlying condition was diagnosed by several experts either as erythroblastosis or as leucemia. Scott and Bowman,[14] in a review of all cases of rupture of the spleen

From the Departments of Pathology, Long Island College of Medicine and Kings County Hospital.

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TABLE I. SUMMARY OF EIGHT CASES OF RUPTURE OF THE LIVER AND THE SPLEEN

CASE NO.	WEIGHT (GM.)	LENGTH (CM.)	AGE	LIVER			SPLEEN		HEMOPERITONEUM (C.C.—ESTIMATED)	FIG.
				WEIGHT (GM.)	ABNORMAL ERYTHROPOIESIS	LESION	WEIGHT (GM.)	LESION		
1	415	28	12 hr.	20		Laceration, hematomas of both lobes anteriorly	1	-	5	
2	730	32	1 hr.	40		Hematoma at border of left lobe	1	-	5	
3	800	36	Stillborn	43		Subcapsular hematoma at coronary ligament and lower surface rt. lobe	1	-	5	
4	1350	42	1½ days	80		Subcapsular tear almost through entire thickness of rt. lobe, probably 2-stage rupture	2	-	20	1-3
5	3140	48.5	Stillborn	145	+	Laceration at edge of left lobe; hematomas on lower surface	10	Laceration at phrenicolienal lig.	15	5
6	3630	53	13 hr.	215	++	Hematomas at coronary and hepatoduodenal ligaments	38	Laceration at phrenicolienal lig.	20	6
7	4300	57	27 hr.	137	+	Hematoma on convexity of left lobe	10	Laceration at phrenicolienal lig.	200	
8	4570	54	Stillborn	347	++	Lacerations at umbilical vein and convexity of left lobe	17	-	20	

in childhood observed in a surgical service over a long period of time, mention none in newborn infants.

The present series of eight cases (Table I) includes five with rupture of the liver, one with rupture of the spleen, and two in which both organs were injured. They were found among autopsies on 121 infants who were stillborn or died during the first three days of life. Cases with hematoma of the liver without hemoperitoneum and those in which rupture had probably occurred after death in utero are not included. The distribution according to size of the infant conforms with that already mentioned. In order to evaluate properly the incidence in infants greater than average size (Cases 6, 7, 8), one must keep in mind that the great majority of all infants examined at autopsy at this hospital are premature. Actually, only sixteen of the 121 infants examined weighed 3,500 Gm. or more.

In two of our patients, the data in Table I should be supplemented by brief notes on the clinical course and autopsy findings.

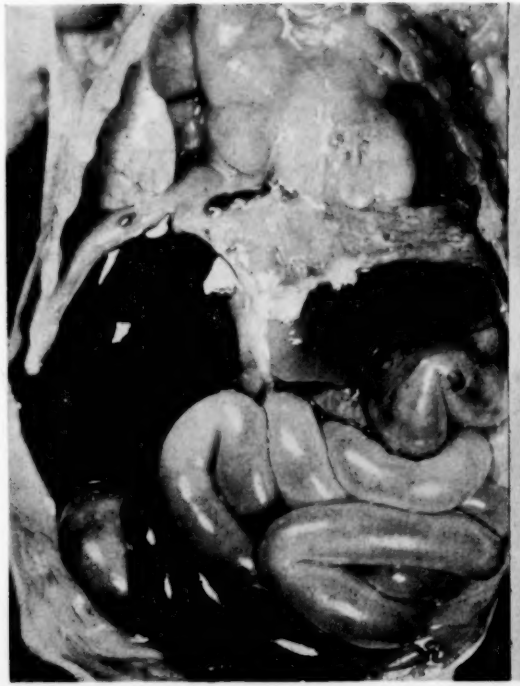
CASE 4.—This infant was born spontaneously and showed at first no abnormalities. The birth weight was 1,410 Gm. At 32 hours of age, the infant suddenly turned pale and limp after being turned and having the diaper changed. No respiration or heart sounds were present. After artificial respiration, cardiac massage, and stimulants, respiration and heart action started again, but stopped soon. In this patient, the findings recorded in Table I indicate very severe trauma to the liver with a small tear in the capsule and a moderate amount of blood in the peritoneal cavity. In view of the history, these findings are best interpreted as the result of a two-stage rupture, the second stage of which had occurred just before death. This seems to be a fairly typical occurrence, and Potter[15] mentions that infants who suddenly die after bath or feeding often have a ruptured subcapsular hematoma of the liver.

CASE 8.—This was the seventh pregnancy of a 35-year-old mother. Labor was slow but progressive. The head was delivered after fifty-five hours of labor. After this the shoulders were fixed in a transverse position at the spines. The head was rotated to the left, and the left shoulder appeared under the symphysis while a snapping sound was heard. The body was delivered with ease to the level of the umbilicus. At this point some difficulty was encountered. The fetal heart was last heard just before delivery. There was no blood group incompatibility between mother and infant. The data in Table I indicate the very large size of the liver in this patient and the locations of the injuries found at autopsy.

The history of the remaining six infants is irrelevant. In no case was the diagnosis of intra-abdominal hemorrhage made during life.

When one reviews the location of the hematomas and lacerations in these eight patients, several distinct types may be found. One is associated with ligaments inserting in the liver or spleen. This is the case in all three instances of laceration of the spleen; in Cases 3 and 6 hematomas are present at the coronary ligament of the liver; in Case 6, also in the hepatoduodenal ligament; and in Case 8, one of the lacerations has a location suggesting that the umbilical vein cut into the liver tissue. In all these cases, the injury can be

Fig. 2.



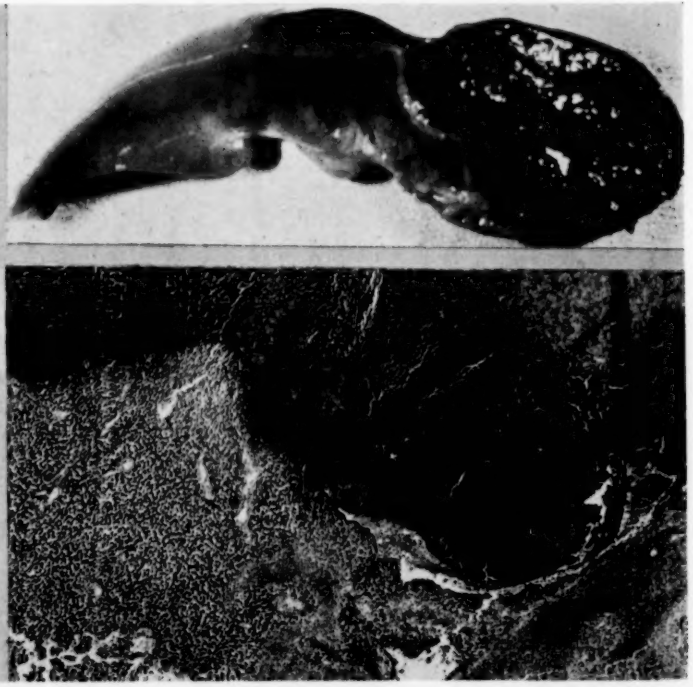


Fig. 1. Fig. 3.

Case 4.

Fig. 1.—The situs of the abdominal organs. The greater part of the right lobe of the liver is dark red in color, and the capsule over it is torn.

Fig. 2.—View of the cut surface of the liver (sides reversed). The dark portion of the right lobe is almost completely separated from the rest of the liver by a deep cleft.

Fig. 3.—A microscopic section of the border area shows the hemorrhagic and necrotic tissue (corresponding to the dark areas in Figs. 1 and 2) in the upper portion, and the normal tissue with a few small areas of necrosis in the lower portion.

explained by a trauma forcing the liver and spleen downward and thus tending to tear these organs off their ligaments.

The location of another group of lacerations on the anterior surface of the liver strongly suggests that the injuries are the result of excessive pressure by the costal margin (Cases 1, 2, 5, 7). This was also found in cases of hematoma without rupture which are not included in the present series. Finally, there are instances in which no specific explanation for the localization of the damage can be given.

Before further discussing the mechanisms by which many of these lacerations may have been caused, a few words should be said about the phrenicolienal ligament. Textbooks of anatomy describe this ligament as inserting at the hilus of the spleen and carrying the splenic vessels. However, examination of the spleen in situ in many newborn infants has shown that the ligament frequently inserts not only at the hilus, but also extends in the direction of the lower pole and sometimes even to the convex surface (Fig. 4). This insertion of the ligament in the spleen itself rather than in the tissue of the hilus apparently predisposes to laceration when the spleen is pulled away from its normal location (Figs. 5, 6).

Fig. 4. Fig. 5. Fig. 6.

Figs. 4, 5, and 6.—Spleen and adjacent portion of the diaphragm, showing the phrenicolienal ligament in a normal newborn infant (Fig. 4), and in Cases 4 and 5 after laceration of the spleen at the insertion of the ligament (Figs. 5 and 6, respectively).

Search for possible circumstances in which liver or spleen may be pulled or pushed downward to the extent of partially tearing off their ligaments has revealed only one plausible mechanism. In the fetus and newborn infants before the onset of regulair air breathing, the diaphragm is at a high level with its domes usually reaching to the third rib or intercostal space. Most of the hollow of the diaphragm is occupied by liver, stomach, and spleen. If the thoracic cage is compressed, these organs are squeezed out of the hollow of the diaphragm and forced downward (Fig. 7). Among the ligaments, the phrenicolienal (*a*) and coronary ligaments (*b*) are obviously under tension when liver and spleen move downward. If the border of the liver is not far from the umbilicus, the umbilical vein (*c*) may cut into the organ when the latter is pushed downward (Case 8). The hepatoduodenal ligament is not likely to be affected

since it runs downward from the liver; yet it showed extensive hemorrhage into its tissue, obviously originating from the liver, in Case 6. Thus, compression of the chest rather than the abdomen explains the majority of the injuries to liver and spleen as found in the present cases, either by direct injury to the anterior surface of the liver (Fig. 7, *e*), or by pushing the organs downward (Fig. 7, *a-d*). On the other hand, those injuries which have no characteristic relationship to ligaments or the costal margin are probably due to a more direct trauma to the liver itself. These cases constitute the minority in our material.

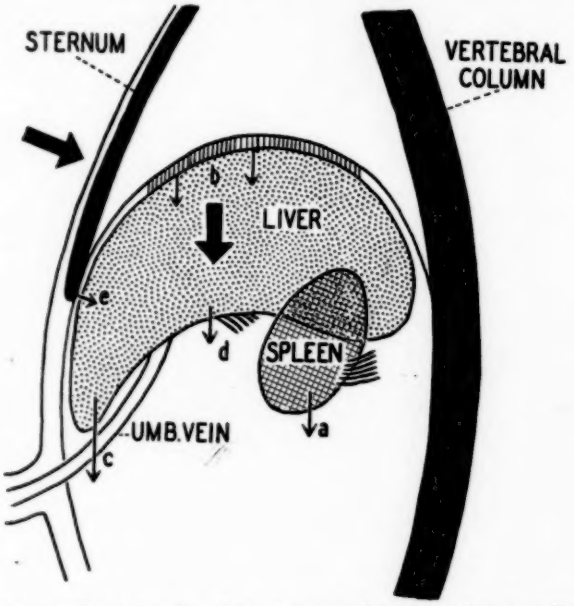


Fig. 7.—Diagram illustrating the effect of compression of the thorax on liver and spleen. As a result, laceration may occur at the following points: *a*, spleen at the phrenicolienal ligament; *b*, liver at the coronary ligament; *c*, the umbilical vein, which may cut into the liver; *d*, liver at the hepatoduodenal ligament; *e*, liver compressed directly by the costal margin.

The relatively high incidence of rupture of liver and spleen in large infants was mentioned above. It should be added that in such children, the liver is often enlarged out of proportion to body size (Cases 6, 8). It is obvious that the mechanism of squeezing organs out of the hollow of the diaphragm will particularly affect a large liver, which may then carry the spleen with it, even if the latter is nearly normal in size. Enlargement of the liver is most commonly found in erythroblastosis and in infants of diabetic mothers. In all three of our infants which were larger than normal, marked hematopoiesis was present in the liver (Cases 6, 7, 8), just as occurs in both erythroblastotic infants and in children of diabetic mothers. Clinical investigation did not reveal any of these patients to be an unequivocal example of either of these; yet, it might be well to remember that erythroblastotic infants and those of diabetic mothers may be more likely to suffer a birth injury to liver or spleen than others.

SUMMARY

The evaluation of findings in eight newborn infants with birth injuries to liver or spleen or both suggests that pressure on the thorax is an important factor in the production of these lesions. By such pressure, the organs of the upper abdomen are squeezed out of the hollow of the diaphragm, and undue tension on the ligaments of the liver and spleen then produces part of the lesions. Others are the result of direct pressure of the costal margin on the anterior surface of the liver. A minority of the lesions of the liver in the present group of cases are not obviously related to these mechanisms and are probably due to direct trauma.

Large infants and those with a relatively large liver as it occurs in erythroblastosis or in maternal diabetes are more susceptible to injury of liver or spleen than others.

In order to prevent these lesions, not only direct trauma to the abdomen but also pressure on the thorax should be avoided as much as possible.

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CHILDHOOD MANIFESTATIONS OF ALLERGIC ADULTS

Prelude to Allergy

Abraham B. Schwartz, M.D.
Milwaukee, Wis.

THE growing child from birth through adolescence reveals frequent recurrent manifestations of disharmony with living experiences. Everyone has witnessed in his own family circle occasional fears or tantrums which represent a child's reactions to the frustrations and drives which harass him. These fears and tantrums are useful devices for protecting the child's integrity in a conflicting world. In the physical field, the human organism possesses an equivalent versatility in reacting to various substances which threaten the specificity of its body proteins. The minor expressions of these reactions are often as mild as are the minor tantrums of the problem child. At other times, the manifestations are violent examples of Pirquet's term "allergy" or altered reaction—a boiling-over, not unlike the childhood neuroses. In the management and control of these, pediatrists and allergists face, in the physical field, the same dilemma which pediatrists and psychiatrists encounter in the mental and emotional field.

The cardinal elements of the allergic design are capillary dilatation and permeability, smooth muscle contraction, and edema. These cellular peculiarities may produce variations in function of one or several organs which earlier clinicians were led to classify as diatheses. Some of these classifications parallel what we now call allergies. Pediatric writing reveals much thinking along this line. Most of this literature antedates the modern period of allergic study, but it is nevertheless obvious that the writers were dealing with what we now call allergic characteristics. In 1902, the year of Richet's memorable experiment, Comby,[1] the French pediatrist, described what he called "arthritism." The signs and symptoms are as follows:

1. Catch cold easily.
2. Subject to nosebleed, more common in summer than winter, spring than fall.
3. Symptoms often related to changes in barometer.
4. Hay fever a later development.
5. Often have large tonsils and adenoids and stridorous breathing.
6. Spasmodic tracheobronchitis.
7. Exaggerated dyspnea with mediocre bronchitis.
8. Perversion and modification of appetite; food dislikes common; geophagia; pica.
9. Intestinal colic.
10. Regurgitation and other varieties of dyspepsia.
11. Cyclic vomiting.
12. Cephalalgia.

From the Department of Pediatrics, Marquette University Medical School.
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While some of the signs and symptoms recorded by Comby seem irrelevant to allergy, the major characteristics of arthritism are unmistakably those of allergic children. Czerny, the renowned German pediatrist, classified a group of symptoms under the heading of "exudative diathesis" (Table I), another illustration of a common pattern seen in allergic children.

TABLE I. EXUDATIVE DIATHESIS OF CZERNY

	PRIMARY SIGNS	SECONDARY SIGNS	ASSOCIATED SIGNS AND SYMPTOMS
Skin	Intertrigo Seborrhea Cradle cap	Eczema Impetigo	Itching Restlessness Disturbed sleep Fears
Mucous membranes	Desquamation and swelling of various organs	Exudative diseases of pharynx and G.I. tract Coryza Laryngitis Bronchitis Blepharitis Phlyctenules Vulvovaginitis	Cough Vomiting Colic Constipation Diarrhea Hay fever Spasmodic croup Asthma Blepharospasm Dysuria Enuresis

The correct interpretation of allergic signs and symptoms may not be reached until long after the symptoms have occurred. In this respect, the single incidents of an allergic history may be not unlike the single takes of a moving picture, in which even the actors are unable to recognize understandable continuity. Each incident begins to make sense only as the whole story is unfolded. Aside from the inadequacies of the story as related by a parent—and there are many—appraisals will differ considerably, depending on what scenes or manifestations the appraiser is willing to accept as part of the story or pattern.

Allergic manifestations generally, and particularly in the child, present many unusual variations in intensity and character. These variations are thought to represent differences in capacity for reacting as modified by genetics, age, and fortuitous differences in environmental experience. Some are easily definable as specific reactions to known allergens; many more seem not unlike the phenomena described by Selye[2] as elements of a general adaptation syndrome, additionally complicated by psychogenic factors. The clue to an allergic diagnosis may therefore be obscured not alone by the wide range of allergic manifestations, but by a variety of complicating mechanisms which accompany biologic phenomena.

For the past few years, I have been reviewing the records of former pediatric patients, now grown men and women. After determining by phone or letter which of these adults had developed allergic symptoms as recognized by their families, clinical inventories were made of their childhood characteristics as recorded in their histories, in an effort to discern a childhood pattern common to those who became allergic subjects. Many of the listed characteristics may lack immunologic validity—that is to say, an antigen-antibody mechanism was not demonstrated. The same characteristics, however, occur frequently enough

in allergic subjects to lend them more than an accidental significance and to form a common pattern. Despite the hematologic discrepancies, "the coat is the coat of Joseph." Although many of the patients used as the basis of this report were easily recognizable as allergic subjects early in life, many others presented no clinical signs regarded as allergically relevant during their childhood. The following signs and symptoms are not necessarily diagnostic signs of allergy. They are the things which happened to allergic subjects in their early childhood. A review of these signs and symptoms shows many characteristics which are by their very nature major allergic evidences. Many others have not been generally recognized as having validity in the early recognition of the allergic personality.

Allergic Characteristics

Digestive Signs and Symptoms

1. Pylorospasm.
2. Enterospasm.
3. Hyperperistalsis—recurrent vomiting, cyclic vomiting, willful vomiting, neurotic vomiting, facility at gagging.
4. Pyloric stenosis.
5. Recurrent abdominal pain (during or between meals), finicky eater.
6. Hypotrophy.

Respiratory Signs and Symptoms

1. Nasal snorting, snuffling, or stuffiness. (Difficulty in breathing, peculiar breathing, fills up with mucus.)
2. Exudative throat (excessive mucus).
3. Congenital stridor.
4. Abnormal frequency of colds.
5. Early adenoid trouble.
6. Allergic salute.
7. Open mouth.
8. Recessive mandible.
9. Nosebleeds.
10. Turgescent mucosa.
11. Excoriated nostrils.
12. Nasal eosinophilia.
13. Hay fever.
14. Recurrent bronchitis.
15. Asthma.
16. Thymic asthma.

Dermatologic Signs and Symptoms

1. Dermatitis neonatorum.
2. Seborrheic dermatitis.
3. Infantile eczema.
4. Urticaria.
5. Atopic rashes. Excessive reactions to sun, insects, dyestuffs in clothing, heat and cold, wool, rubber pants.
6. Dermographism.
7. Canker sores—cheilitis.
8. Vasomotor lability—localized cyanosis of extremities.
9. Hydrolability.
10. Angiospastic pseudoanemia.

Ophthalmic Signs and Symptoms

1. Blepharitis.
2. Recurrent styes or chalazia.

3. Angioneurotic edema.
4. Vernal conjunctivitis.
5. Conjunctivitis—general or focal.
6. Localized pollenosis.
7. Itching—rubbing.

Genitourinary Signs and Symptoms

1. Vaginitis or vulvitis nonspecific.
2. Enuresis.
3. Pruritus.
4. Hydrocele.

Neuromuscular and Psychosomatic Signs and Symptoms

1. Fatigability increased.
2. Night restlessness or fears.
3. Compulsion neuroses.
4. Leg pains.
5. Blue hands and feet.
6. Migraine.
7. "Alarm reactions."
8. Convulsive seizures.

GASTROINTESTINAL CHARACTERISTICS

While the common occurrence of gastrointestinal allergy is well known, the unusual frequency of a disturbed digestive tract in the first few months of life in allergic persons has not been emphasized. In the present study, the occurrence of frequent stools, or loose, foamy, or frothy stools, and hyperperistalsis with or without pylorospasm, were the most common initial manifestations of the allergic constitution in the first three months of life. The hyperperistalsis often showed itself in the first few days of life, accounting for such clinical descriptions as "dyspepsia of the newborn." These symptoms occurred when the infant was a few weeks old and/or after the ingestion of particular foods. In some, the occurrence of temporary periods of improvement followed seemingly unrelated diet changes. Pain may or may not have accompanied the hyperperistalsis. When pain occurred, its severity varied from a mild type, the "under-done" baby of Brennemann, with rhythmical recurrences of discomfort which lent themselves to minor therapeutic measures, to colic severe enough to warrant repeated sedation. The descriptive term "all gut and squall" applies to infants with such severe abdominal pain. While it is not unlikely that some of these infants earned their places in such diagnostic pigeon holes as "underfeeding," "overfeeding," "neuropathic diathesis," "hypertonic infant," "enterospasm," "fat indigestion," and "carbohydrate intolerance," many of them continued discomfited and their pediatrist dissatisfied despite placement in these categories. Among the infancy records of my series, I find such notations as "Breast milk not agreeing," or "Mother reports that infant gags and cuts up generally," or "Screaming spells, vomiting, mucus in stools, fusses after feeding"—this last, in a child who later ran the gamut of allergic experience including a Löffler's syndrome.

In children past infancy, the most significant digestive symptom other than recurrent abdominal pain attacks was an unusual facility at vomiting. The most trifling provocations might elicit gag reflexes, which were easily conditioned by

psychogenic factors. Among this group is the record of a fastidious 4-year-old who, after finishing his meal and quietly announcing "I have to go to the bathroom," would then empty the contents of his stomach into the toilet bowl. A few years later, this child was a major respiratory allergy patient. Recurrent vomiting and cyclic vomiting, a more common diagnosis in former years, undoubtedly belong in this category. The alleged relationship of pyloric stenosis to the allergic constitution finds confirmation in this study.

RESPIRATORY CHARACTERISTICS

Nasal snuffling, snorting, or stuffiness is not uncommonly witnessed in the first few weeks of life. Eliminating those instances explainable by small nasal passages or other anomalies of structure, or explainable by regurgitation of milk curds into the posterior nares, we nevertheless see a considerable number of patients with respiratory symptoms for which there is no obvious explanation. The symptoms appear frequently in the early histories of allergic persons. On clinical records, I find notations such as "difficulty in breathing," "peculiar breathing," "fills up with mucus." An allergic parentage suggests a common etiology for parent and child symptoms. Children with such symptoms are frequently the subjects of early adenoidectomy, an operation which, in the allergic child, will need repeating in later years.

The two most commonly used pediatric texts fail to mention epistaxis as a symptom of allergy. Its frequency in the group of patients studied leads me to believe that, eliminating trauma and blood dyscrasias, epistaxis is more likely due to allergy than to any other cause. As such it may appear even in infancy, long before major allergic signs become apparent.

STATUS THYMICO-LYMPHATICUS

The pathologic relevancy of status thymico-lymphaticus has been a controversial subject for the past two decades. It is now generally believed that simple thymic enlargement is not in itself a cause of so-called thymic symptoms. Sudden deaths without discoverable significant anatomic changes continue to puzzle pediatrists and pathologists. In many patients who die suddenly, a complete clinical inventory often reveals characteristics identified with the hypersensitive state of one or more organs, for which Bohrod[8] proposed the term "sudden death in the hyper-reactor state." Recent investigations have shown the necessity for increased adrenal cortical hormones for survival when the animal organism is exposed to various insults or damage. It has also been demonstrated that excitation of the autonomic nervous system and the release of epinephrine play a significant part in the availability of cortical hormones at these times. Although the common denominator responsible for these defense mechanisms has not been established, it has been adequately demonstrated that the thymus and adrenal play significant roles. This is also dramatically illustrated by Selye's studies on the adaptation syndrome, in which he showed that rapid involution of the thymus and lymph glands with a hyperplasia of the adrenal cortex occur as cardinal features of the so-called "alarm reaction." While Selye's theory has to do with reactions evoked by sudden exposure to nonspecific

stimuli, clinically similar reactions do occur in allergic subjects without demonstrable specific causes. It would be difficult to distinguish between specific and nonspecific causes in the infant organism, whose immature immunologic mechanisms hamper its ability to acquire resistance to stress.

Selye's hypothesis would explain many of the heretofore inexplicable sudden deaths in infants of allergic families, as well as the less critical cases in which collapse occurs without known specific damage or insult. That there is a tie-up between these basic physiologic responses and allergic manifestations has been suggested by numerous observations, as for example by Aldrich's[4] study of the relationship between enlarged thymus, pylorospasm, and vagotonia. The observations by Carr[5] on status thymo-asthmaticus, and by Waldbott[6] on the similarity of the pathologic findings in necropsies of patients with anaphylaxis and asthma, lend credence to the supposition that this relationship is a significant one.

Although it is difficult to evaluate the importance of thymic enlargement as reported roentgenologically in the past three decades, the curious fact remains that an unusually high percentage of those infants in this study on whom the diagnosis of enlarged thymus was made twenty years ago are now the subjects of major allergy.

The varied manifestations of allergic phenomena may be compared to a symphonic pattern in which the respective episodes present themselves in different arrangements, now emphasized by one set of instruments, now by another. The early characteristics represent the prelude to a pattern often not completely developed as a major theme until later life. Pediatrists by successive chronological experiences with otherwise normal children may learn to evaluate the interrelationship of many of the physiologic phenomena now seemingly unrelated, and increase our understanding of the disease patterns in allergic persons.

SUMMARY

1. The allergic design or pattern often begins in infancy.

2. Many of the characteristics of the allergic pattern have long been recognized by pediatrists and classified as "exudative diathesis" and arthritism."

3. A knowledge of the early characteristics of the allergic constitution permits a possible interpretation of many of the symptoms and signs of allergy long before major signs have developed.

4. Attention is called to a few less commonly recognized manifestations in the childhood prelude to allergy.

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PREVENTIVE ORTHOPEDICS IN THE TREATMENT OF POLIOMYELITIS

JOHN F. POHL, M.D.
MINNEAPOLIS, MINN.

POLIOMYELITIS at its onset has the characteristics of an acute infectious disease. The attention of the pediatric or medical clinician is invaluable in preserving life and relieving suffering. Unlike most infectious diseases, poliomyelitis tends to develop permanent aftereffects. The principal observable effects are muscular paralysis and skeletal deformity. The interest which has been centered on weakness or paralysis has tended to obscure the gravity of the problem of deformity. Crippling deformities have been a common aftermath of the disease, often not appearing for months or years after the acute attack. Clinical observations recently presented[1] support the view that poliomyelitis attacks the muscle and fascial tissues directly, in addition to the effect of the disease upon the nervous system.

The suggestion that deformities arise directly from disease of the peripheral tissues as part of the acute illness implies the possibility that treatment of the peripheral tissues may reduce or prevent deformity. The underlying cause of deformity has been one of the primary studies in a series of 1,775 patients which have come under the care of this clinic since 1940. The practical aspects of relief and prevention of deformity by treatment of the affected peripheral tissues in this large series of cases is the subject of this presentation.

The patients were admitted with acute poliomyelitis during the various poliomyelitis seasons, beginning in 1940 and extending through 1946, and have been closely followed. Thus, the early aspects of the disease as well as the late effects in the treated patients have been scrutinized.

A serious epidemic of poliomyelitis struck Minnesota in 1946 and provided an opportunity to study the effect of the disease upon the peripheral tissues of 1,125 patients treated in that single year. A mortality of 6 per cent (68 patients) indicates that the disease in 1946 was not mild, but was at least of average severity. In 65.4 per cent (736) of the patients, there was evidence of muscle weakness or paralysis at the height of the disease, but 34.6 per cent (389) of the patients showed no muscle weakness or paralysis at any stage. In every patient in the acute stage it was possible to demonstrate that tissues in the various peripheral parts were involved in a condition of spasm, marked usually by pain and sensitivity.[2] Muscles in spasm were shortening, and in many of these acutely ill patients incipient deformities were already being produced by the shortening muscles. (See Table I).

The general plan of management[3] which was carried out in 1946, as in the previous years, was to hospitalize every patient until spasm and muscle

From the Elizabeth Kenny Institute, Minneapolis, Minn.

TABLE I. INCIPIENT DEFORMITIES FROM MUSCLE SPASM AT THE HEIGHT OF THE DISEASE IN 1,057 SURVIVING PATIENTS WITH ACUTE CASES OF POLIOMYELITIS OF ALL TYPES FROM THE 1946 EPIDEMIC IN MINNESOTA

DEFORMITY	NUMBER OF DEFORMITIES
Torticollis	6
Scoliosis	19
Lordosis	43
Cupped shoulder	25
Tilted pelvis (apparent leg shortening or lengthening)	72
Leg torsion	63
Flexed hip	19
Flexed knee	33
Equinus foot	14
Varus foot	17
Valgus foot	8
Cavus foot	33
Other deformities	43
Total deformities	395

shortening had been overcome and each patient had also been retrained as thoroughly as possible in the normal motor patterns. Treatment of the peripheral tissues consisted primarily of complete rest in bed with prompt and intensive application of moist heat to all areas affected by spasm. As pain and sensitivity disappeared, gentle manipulation and manual release of the shortened tissues was used where necessary in conjunction with the moist heat. Incipient deformities from muscle shortening responded to this treatment as spasm was overcome. Nine of the patients from the 1946 series remain hospitalized for early deformity at the time of this report, but eventual relief can reasonably be expected, on the basis of past experience, by further treatment of these severely affected patients. A possible exception is that of a 6-year-old boy with scoliosis from marked spasm of the spinal muscles, occurring early in the acute stage of the disease and which has responded poorly. The distortions still present, but under treatment, are: four patients with scoliosis, two patients with lordosis, two patients with equinus foot, and one patient with varus foot. At this time, more than a full year after the epidemic, 1,048 of the 1,057 surviving patients are free of gross deformities.

Every patient has been treated for spasm in order to avoid tissue fibrosis and contractures, which have been a cause of late deformity in the growing child. The tendency for contracture of the fascia lata and iliotibial band of the thigh has been particularly vexing in the past and has been a common source of late-appearing deformity. Prevention of future deformity depends apparently upon the successful relief of spasm.

The period of hospitalization of the 1,057 surviving patients of the 1946 epidemic averaged twenty-one days for the thirty-three patients with abortive cases (those with clinical symptoms other than paralysis, but having a normal spinal fluid cell count); twenty-three days for the 356 nonparalytic patients; and will average from two to fourteen months for the paralytic patients, depending upon the severity of the attack. It is estimated that nine patients will require a stay of two years.

Muscle spasm as well as attendant deformity were not found to be confined to the paralytic patient. Spasm is usually more severe and more difficult to

relieve in the paralytic type of case. This is indicated in part by the increased time required for adequate treatment of the paralytic patient. The greater frequency of deformity in the paralytic case undoubtedly has led to the belief that deformities arose from paralysis. Incipient deformities in the series presented here responded to treatment of the peripheral tissues in the paralytic as well as the nonparalytic patients. Once relieved, the deformities have not recurred in spite of weakness and muscle imbalance present in the paralytic patients. New deformities have not developed in the patients who have completed treatment. These observations provide evidence that disease in the peripheral tissues rather than the unbalanced pull of muscles causes deformity. Two representative case histories from the 1946 series reported in this paper illustrate this point.

CASE REPORTS

CASE 1.—R. N., an 8-year-old boy, became ill July 23, 1946.

Diagnosis.—Poliomyelitis, acute, paralytic type.

Spinal Fluid Examination.—Cells 90 per cubic millimeter; protein 75 mg. per cent.

Physical Examination.—At the height of the disease there was spasm of the neck, back, hamstring, and calf muscles, and shortening of the iliotibial band and plantar fascia. The incipient deformities of scoliosis, pes varus, and pes cavus were evident. The right arm and right leg were mildly weakened, the left leg was completely paralyzed, and the back and abdomen were severely paralyzed at the height of the disease.

Outcome.—Aug. 25, 1947, when the patient was discharged, walking, after 394 days of hospitalization, the muscle shortness was relieved. The left leg and abdomen were still severely paralyzed. There were no deformities at the time of discharge. On Feb. 1, 1948, examination showed paralysis of the left leg and abdomen still present. No deformities have developed. No apparatus is worn. The incipient spinal deformity has been relieved in spite of permanent residual paralysis of the abdomen.

CASE 2.—R. R., a 14-year-old boy, became ill on Aug. 3, 1946.

Diagnosis.—Poliomyelits, acute, nonparalytic type.

Spinal Fluid Examination.—Cells 62 per cubic millimeter; protein 65 mg. per cent.

Physical Examination.—At the height of the disease there was spasm of the neck, back, hamstring, calf, and quadratus lumborum muscles, and shortening of the iliotibial band of the thighs. The incipient deformities present were: tilted pelvis with lumbar scoliosis, an apparent right leg shortening, and a right heel inversion. This patient at no stage of the disease showed any evidence of muscle weakness or paralysis.

Outcome.—On Aug. 30, 1946, when the patient was discharged after twenty-seven days of hospitalization and treatment to the peripheral tissues, all muscles were of full length and there was no evidence of deformity. No paralysis was present. On Feb. 1, 1948, examination showed a fully recovered patient. No deformities or paralysis were present.

Experience with the 650 patients admitted from 1940 through 1945 shows that gross late deformities have not occurred in the treated patients. Growth in length of limbs affected by the disease has proceeded satisfactorily. Retardation of growth, noticed in the past, has apparently been due to shortened muscles.

No operations have been performed or are known to have been applied to any of the patients. It is possible that cases may appear where function of a part can be improved by transplantation of a muscle, but no practical instance has so far arisen.

Scoliosis has been kept to a minimum. This has been most satisfying in view of the seriousness of spinal deformity and its frequency of occurrence in the past. Colonna and Vom Saal[4] reported the incidence of scoliosis to be 30 per cent in a series of 500 chronic, paralytic cases of poliomyelitis. There are three instances of gross permanent scoliosis in the 650 patients treated in this clinic from 1940 through 1945. All occurred in the acute stage of the disease and could not be relieved. These patients are worthy of note.

Patient D. L., a young boy, was admitted in October, 1944, at the age of 13 years, with severe spasm affecting particularly the back and legs, and with arms extensively paralyzed. After 572 days of hospitalization he was discharged, but he retained at that time moderate back stiffness and a minimal scoliosis that could not be relieved in spite of intensive treatment to the peripheral structures. He is examined periodically, and while the scoliosis eventually showed a 2-inch deviation of the spine it is not progressing in this boy, who is now 17 years of age.

Two of the young patients just mentioned are girl cousins and were both admitted to this clinic in November, 1945, with severe paralytic type of poliomyelitis. Spasm was extensive throughout the body and was particularly painful. Patient D. D. had incipient right mid-dorsal scoliosis early in the illness but did not respond to intensive treatment. The patient was discharged after 255 days of hospitalization in the belief that the scoliosis might have antedated the poliomyelitis. Within six months from the time of discharge the scoliosis had become much more severe, indicating that it was, after all, poliomyelitic in origin. The patient was readmitted to the hospital for 198 days of further treatment. The scoliosis is still present (2½ inch deviation of the spine) and cannot be relieved. Patient V. D. developed a left lumbar scoliosis in the acute stage of the disease, due to severe painful spasm of the right spinal and abdominal muscles. The scoliosis has remained minimal (⅞ inch deviation of the spine) and appears nonprogressive, but it has not been possible to relieve the muscle shortening causing the scoliosis in 483 days of hospitalization. Another cousin, C. D. (sister of D. D.), was hospitalized with nonparalytic poliomyelitis at the same time as the other two. This patient developed an incipient lumbar scoliosis due to shortening of the quadratus lumborum muscle. The condition was relieved after thirty-one days of hospitalization and has not recurred in the fourteen months since the patient was discharged. It is believed that the two cases of permanent spinal deformity in these cousins resulted from the extremely severe nature of the spasm, as both patients experienced excruciating pain in the acute stage.

The symptoms of disease in the peripheral tissues have been recorded by many observers. Lovett[5] recognized that the peripheral tissues were tender in the acute stage of poliomyelitis, but from his writings he did not apparently connect this fact with deformity. Ober[6, 7] pointed out that there was pain deep in muscles in poliomyelitis which was productive of deformity. Miss Kenny was first in establishing muscle spasm as a distinct entity in the disease, and at one time[8] explained this condition as due to a zone of irritation in the spinal cord. Subsequent investigation[1] indicates that the peripheral tissues of the body

are directly assaulted by the malady. The painful muscles are diseased and shorten themselves if unattended. These observations provide a reasonable clue to the major problem of deformity in poliomyelitis.

Paralysis or motor denervation of muscle is a feature of poliomyelitis. The evidence is convincing that the disease destroys anterior horn cells of the spinal cord in some cases. There is presently no known method of resurrecting these dead nerve cells; therefore, weakness or paralysis must be accepted as permanent in patients exhibiting residually this condition. The management of paralysis requires its own techniques. No clinical or experimental proof has ever been reported to show that deformities arise directly from muscular paralysis or unbalanced muscle pull.

The orthopedic surgeon is concerned with the preservation of structure as well as function of the locomotor system of the body. Poliomyelitis deformities are crippling in themselves, and they add disability to the paralytic patient. The past role of the orthopedic surgeon in poliomyelitis has been largely to correct chronic deformities and to aid the recovery of muscle function through reparative or surgical means. Prevention of aftereffects of disease is a basic principle in orthopedic surgery as it is in the entire field of medicine. From the beginning of poliomyelitis, the orthopedic surgeon and the pediatric or medical clinician working together must be on the alert for prevention and relief of contractures and deformities arising from disease of the peripheral tissues.

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Case Reports

DIAGNOSIS AND TREATMENT OF PANCREATIC CYSTS IN CHILDREN WITH REPORT OF A CASE

LIEUTENANT T. C. MCPHERSON, MEDICAL CORPS, ARMY OF THE UNITED STATES, AND H. SIDNEY HEERSMA, M.D.
KALAMAZOO, MICH.

SOLITARY cyst of the pancreas, rare in adults, is so exceedingly rare in children as to be almost a collector's item. Moynihan,[1] writing in 1902, noted that of Korte's collection of 121 cases in 1898, only two were in children: Richardson's[2] case in a 14-month-old infant, and Shattuck's[3] case in a 13-month-old infant in whom the tumor had been noticed at birth. Telling and Dobson[4] reported a case in an infant in 1909. Eha,[5] in 1922, reported a case in a child in which the cyst was composed of two distinct sacs. His patient was a 5-month-old female infant. The cyst was 9 cm. in diameter, weighed 99 Gm. and was completely excised at operation. Judd and his associates[6] mentioned the case of Railton,[7] reported in 1896, in a 6-month-old infant. Judd reviewed forty-seven cases seen at the Mayo Clinic from 1921 to 1930, occurring in persons between the ages of 20 and 72 years. Drennan[8] reported a case in a child in 1922. Friedenwald and Cullen[9] in 1926 reported seven cases of pancreatic cyst from the Johns Hopkins Hospital, including Lewis' case, that of an infant 16 months of age, in whom the cyst was of large size, containing 750 c.c. of fluid. This cyst was treated by incision and drainage, and marsupialization of the cyst to the abdominal wall.

The case here presented is that of a 6-month-old infant with, relatively, a very large cyst, which none the less was susceptible to extirpation.

CASE REPORT

J. M., aged 6 months, was admitted to Bronson Methodist Hospital in Kalamazoo on Nov. 27, 1947, because of abdominal distention with fever and vomiting. He had had a cold for three days prior to admission and had vomited once the day before admission, but abdominal distention was not noted by the parents until the day of admission, when he again vomited. On close questioning it developed that the infant had had an episode of distention and emesis at the age of one month, but it was of short duration and self-limited. Delivery was normal following an uncomplicated full-term pregnancy, there was no history of trauma at birth, and the neonatal period was normal. Feeding and developmental history were normal. The family history was entirely noncontributory; there was one sibling, living and well.

Examination on admission revealed a white male infant of size and appearance commensurate with the stated age. The weight was 17 pounds, 9 ounces. The rectal temperature was 102.6° F., blood pressure 94/60, pulse 140, and respirations 44. The skin was warm and dry with normal turgor, but slightly pale. There was no palpable lymphadenopathy. The head was of normal contour, and palpation revealed no abnormal defects in the skull, nor was a bruit heard over the skull. There was a profuse mucopurulent nasal discharge. The tongue was coated with greenish yellow matter. The posterior pharynx showed

only mild injection. The ears were normal. Extraocular movements were apparently normal, pupillary reflexes were active, and ophthalmoscopic examination revealed normal fundi. Respirations were chiefly thoracic, and the chest was nearly fixed in inspiration. Respiratory movement was abnormally slight, but the lung fields were clear to auscultation and percussion. Examination of the heart was essentially negative, though there appeared to be slight enlargement to the left. The abdomen was markedly distended, and the diaphragm was elevated. A tympanitic percussion note was marked over the entire right half of the abdomen, but the note was definitely dull on the left side, with a rather sharp line of demarcation approximately midline. Occasional borborygmus was audible over the right side. The liver was not palpable on the right. Palpation of the left half of the abdomen revealed a cystic mass occupying almost the entire left side; the mass was smooth, extended almost to the floor of the pelvis, and was slightly tender. A definite border could not be felt in any direction. The bladder was not distended. No other masses were felt. The mass was not palpable on rectal examination. The external genitalia and the extremities were normal. Tendon reflexes were normal; abdominal reflexes were absent.

Laboratory Data.—On admission, hemoglobin was 8.2 Gm., the red blood count 3.43 million, and the white blood count 15,300 with 80 per cent neutrophiles, 19 per cent lymphocytes, 1 per cent monocytes. Urinalysis was normal except for 4 plus acetone. Blood sugar was 63.7 mg. per cent, the carbon dioxide combining power was 36 volumes per cent, total protein 5.8 Gm. per cent, the albumin-globulin ratio 1.5. Unfortunately, a serum amylase determination was not obtained. However the serum amylase level eight days postoperatively was 144.1 mg. glucose per 100 ml. blood serum, which is within normal limits.

Possible diagnoses considered at this time were enteric cyst, mesenteric cyst, omental cyst, renal cyst, adrenal cyst, hepatic cyst, splenic tumor, pancreatic cyst, and cyst of the retroperitoneal lymphoid tissue, with the possibility that in any case the mass might be malignant with cystic degeneration.

Roentgenograms.—

Chest: November 27—Moderate enlargement of the heart to the left, with prominence of the left auricle, and pulmonary artery shadow. Lung fields clear. Both leaves of the diaphragm are quite high.

Abdomen: November 27—Minimal distention of small and large bowel and stomach. Large soft tissue mass occupying the posterior half of the left abdomen. Practically all of the intestinal shadows are in the right half of the abdomen.

I. V. Pyelogram: November 28—Good concentration of the dye by both kidneys. Slight dilatation of the left renal pelvis, probably due to extrinsic pressure on the lower left ureter.

Barium enema: November 28—Colon lies mainly anterior and in the right abdomen.

Impression: Extra-alimentary, extrarenal tumor.

Course.—The temperature responded fairly well to parenteral fluids and penicillin, but occasionally rose to 103° F. during the preoperative course. Distention was considerably relieved by Wangensteen drainage. Fluid and nutritional requirements were maintained by intravenous and subcutaneous infusions of glucose, Amigen, and vitamins. The patient received whole blood transfusions of 100 c.c. on the second, 45 c.c. on the third, and 100 c.c. on the fourth hospital days. On the fifth day the hemoglobin was 12.4 Gm., the red blood count 3.94 million, the white blood count 21,000, with 75 per cent neutrophiles and 25 per cent lymphocytes.

On Dec. 2, 1947, the sixth hospital day, the patient was taken to the operating room, continuous intravenous drip started by cut-down on the saphenous vein, and, under open drop ether anesthesia, the cyst removed. Through a transverse incision above the umbilicus the operator first dissected the retroperitoneal space on the left side, back almost to the vertebrae, without encountering the tumor. The peritoneum was then opened, and the cyst, about 16 cm. in diameter, filled the incision. The cyst was enveloped in the gastrocolic ligament, which was drawn taut over its surface. The stomach was displaced upward, and the colon forward, down, and to the right by the cyst. The wall was loosely adherent to the stomach anteriorly and to the duodenum posteriorly. The pedicle was quite small, and it was possible to remove the cyst intact by ligation of the pedicle. It was found that most of the body of the pancreas was removed with the cyst, leaving the tail and the head. A soft rubber drain was placed through a stab wound low on the left side, and the operative incision was closed. The patient received 200 c.c. of whole blood during the operation and the next twelve hours.

The duodenal drainage was continued for two days postoperatively, and was not necessary after that time. The wound drained yellow and then yellowish green fluid for one week after operation; then the drain was removed, and the stab wound healed readily. The postoperative course was essentially uncomplicated except for a temperature rise to 102.8° F. on two consecutive days twelve days after the operation, but signs of an upper respiratory infection were found at that time, and the temperature responded promptly to penicillin and symptomatic therapy. Blood sugar determination on December 10 was 82.9 mg. per cent. The abdomen remained flat, and the infant was discharged two weeks after operation, in good condition, taking his feedings well. The weight at discharge was 15 pounds, 14 ounces.

Pathology.—The moderately tense cyst, 16 cm. in diameter, contained 1,000 c.c. of cloudy yellow fluid. The cyst was unilocular. The wall was soft, flexible, 2 to 4 mm. thick, and contained two soft lymph nodes 7 mm. in diameter in the subserosa of the portion which had been attached near the tail of the pancreas. A sheet of ragged turbid fibrin clung to the inner surface of the posterior wall. Microscopically, the cyst wall was found to have no epithelial lining. All parts of the wall showed a hyaline fibrous tissue structure, with varying degrees of edema and lymphocytic infiltration, and remnants of pancreatic structure. The pedicles were found to be pancreatic tissue with excessive fibrous stroma and dilated small ducts. The specimens of pancreatic tissue, taken separately at operation, showed a few islets and marked increase of fibrous stroma, with lymphocystic infiltration. The cyst fluid contained many neutrophiles and some red blood cells, but no organisms, few cholesterol crystals. Amylase was present in a concentration a little greater than that normally present in saliva. Trypsin was not found.

Pathologic diagnosis: Pancreatic cyst, possibly of inflammatory origin. Pancreatic fibrosis, possibly related to a general fibrocystic disease of the pancreas.

DISCUSSION

The classification of pancreatic cysts, clearly stated by Moynihan[10] and reemphasized by Mayo-Robson and Cammidge[11] in their monograph on the pancreas, has since been subjected to considerable muddling, and has suffered in passage.

Classification of Pancreatic Cysts.—

1. Retention cyst, due to obstruction in the pancreatic duct, smaller ducts, or acini.

2. Proliferation cysts (cystadenoma and cystepithelioma). Castleman[12] prefers the term cystoma to cystadenoma, because he does not believe there is real formation of glands in these tumors.

3. Congenital cystic disease.

4. Hydatid disease, or parasitic cysts (echinococcus cysts).

5. Pseudocysts, including Moynihan's hemorrhagic cysts, all of which are produced by trauma or degenerative changes of the interstitial tissue of the pancreas. They are distinguished from "true" cysts in that they are not within the substance of the pancreas but lie outside of the pancreas, usually in the lesser omental sac or the gastrocolic ligament. They have no epithelial lining. They are frequently preceded or accompanied by acute or chronic pancreatitis, or hemorrhagic pancreatitis.

6. Dermoid cysts of the pancreas (added by Primrose[13]).

Pathologically, the first three types are "true" cysts and the last three are "false" cysts. However, such a division is of little value from the therapeutic point of view.

Symptoms.—In infancy the symptom that brings the patient to the physician most frequently is the abdominal enlargement; a palpable tumor was present in 114 of Korte's[14] 121 cases. Persistent vomiting and loss of appetite —signs of obstruction, partial or complete—are even more striking, but usually occur later, when the size of the cyst is sufficient to cause obstruction by compression of the small intestine. In our case the parents of the infant denied having noticed any abnormal enlargement until a day or two before the infant was brought to our attention, but this was more probably on account of parental ineptitude than any sudden increase in size of the cyst, as the fluid contained in this cyst was not grossly bloody, and the blood supply of the cyst wall was well adapted to the size of the cyst at the time of operation. While precursory or concomitant conditions of the pancreas may give rise to signs of disturbed pancreatic function, symptoms of pancreatic cyst per se are due to a mechanical disturbance of neighboring viscera rather than to alterations in the pancreas itself.[15]

Diagnosis is based on enlargement of the abdomen, with or without signs of intestinal obstruction; the exculpation of other intra-abdominal cysts, chiefly by roentgenography; and by the characteristic roentgenologic findings of pancreatic cyst. In pseudocyst, in addition, the serum amylase level is frequently elevated above normal.[16] Case[17] has given us an excellent survey of the roentgenologic aspects of pancreatic cyst, to which the reader is referred for a comprehensive handling of this matter. Suffice it to say that intravenous pyelography will ordinarily reveal a normal urinary tract, and that gastrointestinal series of x-ray pictures following barium meal and barium enema will reveal displacement of the stomach upward or forward (in a smaller cyst), and of the colon and small intestines downward and to the right side of the abdomen, by a mass of homogeneous opacity with smooth round borders. Gastric pneumograms are also of value. Differential diagnosis in children should exclude adrenal, ovarian, mesenteric, enteric, omental, and hepatic cysts, hydronephrotic or cystic kidney, perinephritic abscess, Wilms' tumor, splenic tumors, and retroperitoneal tumors and cysts.

Treatment has not been altered radically since Moynihan[1] summarized the possible procedures as: (1) aspiration (Recomier's method), which is not recommended; (2) evacuation and drainage, with marsupialization of the cyst; (3) extirpation, which he did not consider feasible in most instances. Judd[6] is of the opinion that "the ideal treatment is complete removal, if possible. . . ." He recommended it only for small cysts with few adhesions, but in the same paper cites Bozeman's[18] case, reported in 1881, in which a cyst weighing 20½ pounds

was successfully extirpated. It is generally agreed now that whenever the condition of the patient and the situation and mobility of the cyst are favorable, the cyst safely may be removed en masse. Most of the authorities have recommended aspiration of the cyst prior to extirpation at the time of operation, but in our case the surgeon found it easier to deal with the distended cyst.

If extirpation is performed, the area should be drained, preferably through a separate stab wound. Drainage should cease within ten days or two weeks at most. If a marsupialization operation is performed, the sinus tract may close within about two weeks at best,[7] or may persist or recur for extended periods of time. Persistent sinus tract may be obliterated by anastomosis with the stomach or small intestine.[19]

Prognosis is good if the operation is timely and the postoperative course is uncomplicated. From a prognostic point of view, extirpation probably offers the best outlook, when this method of treatment is possible.

Possible association of a large solitary cyst of the pancreas, such as we have seen, with generalized clinical fibrocystic disease of the pancreas is purely a speculative subject. At last report, two months after operation, our patient was in excellent condition and gaining weight normally, with no intervening illness. It is planned to take samples of duodenal contents later, to determine the presence or absence of pancreatic enzymes.

According to the pathologist's report, this cyst probably should be classified as a pseudocyst of the pancreas. However, the inflammatory changes found in the wall of the cyst may well have been secondary, and the very presence of remnants of pancreatic structure in the cyst wall suggests the possibility that this cyst may have developed as the result of obstruction of one or more ducts, which would place it in the class of retention cyst—a very large one which had outgrown the pancreas, and in which the lining epithelium had been destroyed by pressure of accumulating fluid.

SUMMARY

1. A brief review of the literature reveals seven cases of solitary cyst of the pancreas reported in children, chiefly in infants.

2. A case of a very large solitary cyst of the pancreas is reported in a 6-month-old male infant, in which the cyst was treated by surgical extirpation.

3. An attempt is made to clarify the classification of pancreatic cysts, and diagnosis and surgical treatment methods are discussed, with the recommendation that wherever possible extirpation is the treatment of choice.

4. The possibility of association of some pancreatic cysts with cystic fibrosis of the pancreas is raised for speculation.

The patient was referred by Dr. W. McFadden of Bloomingdale, Mich. Dr. M. Peelen performed the surgery. The pathologic report was furnished by Dr. Hazel Prentice.

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ERYTHEMA MULTIFORME WITH PLURIORIFICIAL LESIONS AND SYSTEMIC MANIFESTATIONS

Report of a Case With Recurrence of Mucous Membrane Lesions

Joseph A. Ritter, M.D., Theodore M. Ginsburg, M.D., and
Emanuel Berger, M.D.
Philadelphia, Pa.

VON HEBRA[14] in 1866 separated from an ill-defined group of erythemas an entity which he called erythema exudativum multiforme. Kaposi[6] subsequently described a form of the disease in which mucous membranes were involved, and Rendu[11] noted cases with fever and constitutional symptoms. Keil,[7] in reviewing the historical background of the disease, credited Bazin[1] with describing in 1862 the syndrome associated with severe eye complications and stomatitis. In 1922 Stevens and Johnson[13] reported two cases of "a new eruptive fever associated with stomatitis and ophthalmia." The type of erythema multiforme described by these observers appears to be identical with that earlier reported by Bazin, but the syndrome has come to be known as "Stevens-Johnson's disease." Since their initial report in 1922, approximately seventy other cases have been recorded in the American literature. At the present time, forms of the disease are recognized in which the gastrointestinal and genitourinary tracts, mediastinum, pulmonary system,[3, 10, 12, 15] and meninges[8] are also involved.

Erythema multiforme of the type originally described by Bazin and by Stevens and Johnson is characterized by an insidious onset with mild conjunctivitis and stomatitis followed in a day or two by any of the skin eruptions of erythema multiforme. The latter may become vesicular, bullous, or hemorrhagic. Fever and systemic symptoms are usually present in variable degree, depending upon the progression and severity of the skin and mucous membrane lesions. The periorificial areas are swollen and hyperemic, often fissured and hemorrhagic, with crust formation and desquamation. Sometimes anal and vaginal synechiae result. Marked ulceration of the mucous membranes may ensue with sloughing, pseudomembrane formation, and bleeding. Although the oropharynx[5] and pulmonary system may be involved, the oral and eye lesions are the most striking phenomena encountered.

In mild cases the conjunctival mucous membranes may show only slight erythema, but in severe cases purulent exudate with marked erythema and edema of the lids and even hemorrhage, ulceration, and desquamation may occur. Sloughing of the bulbar and palpebral conjunctivae sometimes follows. The involvement of the eyes may extend beyond the mucous membranes, and panophthalmitis occasionally results. Pseudomembranous formations at times produce keratoconjunctivitis sicca with perforation of the cornea. Chronic conjunctivitis, synechiae, symblepharitis, corneal scarring, and blindness have been observed as sequelae.

The case herein reported was considered to be of interest because of the recurrence of mucous membrane lesions four months after the initial onset. Of additional interest were the investigations pertaining to viral etiology.

CASE REPORT

A 22-month-old female infant was admitted to the Pediatric Department of the Graduate Hospital of the University of Pennsylvania on March 31, 1947,

From the Department of Pediatrics of the Graduate Hospital of the University of Pennsylvania.

because of fever, swelling of the eyelids, blood-streaked saliva, and an urticarial-like skin eruption of two days' duration. On March 18, 1947, the patient had been seen at home by one of us because of rhinorrhea and a dry cough accompanied by slight fever. The mother and brother of the patient had recently recovered from an upper respiratory infection which was epidemic at the time. The patient was treated with a mixture containing codeine phosphate, acetylsalicylic acid, potassium citrate, syrup of ipecac, and syrup of chocolate during the day, and phenobarbital at bedtime. She made an uneventful recovery in a few days. Twelve days after the onset of her illness there suddenly developed a generalized urticarial-like eruption with fever, marked swelling of the eyelids, and swollen, erythematous bleeding gums. Elixir of Benadryl was prescribed. The following day symptoms were accentuated and she was hospitalized.

The patient was born spontaneously at term, weighing 6 pounds, 14 ounces. She was jaundiced for about two weeks following birth and was given small blood transfusions. The mother was Rh negative and the infant, Rh positive. The mother's blood, examined by Dr. Neva M. Abelson during the patient's present admission, showed a low titer of Rh-blocking antibodies. The developmental history of the child was quite normal. She had three attacks of tonsillitis at one year of age and had received the usual immunizations including smallpox vaccination.

Physical examination on admission revealed an acutely ill, well-nourished, irritable infant, with red, edematous, tightly shut eyelids and swollen lips. There was a large hemorrhagic bleb on the lower lip. On the trunk, face, upper extremities, and thighs were scattered and confluent scarlatiniform, morbilliform, and vesicular lesions. Confluent lesions were most prominent on the anterior aspects of the thighs. The palms were involved but not the soles of the feet. When the eyelids were opened with a lid retractor, a clear fluid, under considerable pressure, was found. The corneas were somewhat dulled, and the conjunctivae were congested and edematous. A slough which bled easily covered the oral mucous membranes. The tongue was thick and heavily furred. Saliva mixed with blood and debris drooled constantly. The vagina and anus showed marked hyperemia with sloughing of the mucous membranes and adjacent skin. Superficial lymph nodes were moderately enlarged in the cervical area. A few scattered coarse rhonchi were heard over the lungs. There was no impairment on percussion. The heart was normal in size, and the sounds were of good quality. The spleen was not palpable, but the liver extended about one centimeter below the costal margin on deep inspiration.

On admission, 500 c.c. of 5 per cent glucose in saline was administered intravenously. Penicillin in a dosage of 100,000 units was given intramuscularly every three hours. During the first twenty-four hours she also received 300 c.c. of citrated blood. Nourishment by mouth was impossible during the first seventy-two hours because of the acute oral inflammation. When oral feeding could be instituted, a diet consisting of a mixture of half skimmed milk, ascorbic acid, eggs, vitamin B complex, vitamins A and D, Dextri-Maltose, and casein hydrolysate was given. The conjunctival sacs were flushed with boric acid solution and penicillin (5,000 units per cubic centimeter) instilled alternately every two hours. One drop of one per cent homatropine and penicillin ophthalmic ointment were employed locally in each eye three times daily. Three days later this was changed to ¼ per cent scopolamine, one drop daily, and mineral oil instillation alternating with penicillin drops every two hours. The genitalia were flushed several times daily with boric acid solution followed by mineral oil. Petroleum jelly gauze strips were applied to the orificial skin.

A blood count on admission revealed 18,200 leucocytes with 79 per cent neutrophiles, 15 per cent lymphocytes, and 6 per cent monocytes. The platelet

count was 489,720 cells per cubic millimeter of blood. A blood culture taken on the day of admission revealed no organisms.

On the third hospital day the cutaneous lesions were typical of erythema multiforme iris. Distributed over the trunk, face, arms, forearms, hands, and the anterior surfaces of the thighs and legs there were vesicles and bullae in the center of large edematous papules. The eyelids were congested, and the left lid was desquamating. The lips were severely hyperemic and showed necrotic areas and bloody debris. The oral mucous membrane appeared to be sloughing, and the tongue was thick and furred. The vagina was swollen, hyperemic, and desquamating. The anus and perianal areas were erythematous and sloughing. The chest revealed mild suprasternal and intercostal retraction on inspiration. The clinical picture was alarming.

The leucocyte count remained within normal limits, and there was no increase in heterophile antibody titer. Cephalin flocculation, thymol turbidity, and colloidal gold tests were within normal limits. Total serum proteins were 6.64, albumin 4.05, and globulin 2.59 Gm. per cent respectively. Total serum cholesterol was 194 mg. per cent, and cholesterol esters measured 142 mg. per cent. Culture from the left eye revealed nonhemolytic streptococcus and from the right eye, hemolytic *Staphylococcus albus*, coagulase negative. Throat and mouth cultures, both by aerobic and anaerobic techniques, yielded *Streptococcus viridans, Streptococcus haemolyticus,* and diphtheroids.

Fig. 1.—Fifth day. Eyelids and lips covered with bloody crusts.

The skin lesions on the fifth day appeared dusky red, with hemorrhage in some of the vesicles and bullae. The eyelids were less edematous but continued to be covered with bloody crusts (Fig. 1). The palpebral conjunctivae were covered with a soft, fibrinous membrane, which hung loosely in each eye. Both the bulbar and palpebral conjunctivae had a granular appearance. The leucocyte count was 12,000 cells per cubic millimeter of blood with 75 per cent neutrophiles. By the eighth day the child began to take adequate amounts of fluid, in spite of the fact that the lips and mouth continued to bleed. The eyes could be opened, the corneas were clear, and the lids covered with bloody crusts. Many of the skin lesions had begun to dry and crust (Fig. 2). Thereafter, improvement was continuous. The child became less fretful, and the temperature began to fall by lysis. The older skin lesions showed definite signs of involution. Twelve days after admission total serum proteins were 6.48, albumin 3.72, and globulin 2.76 Gm. per cent respectively. Flocculation tests were repeated and found again to be normal.

An intravenous infusion, on the fifteenth hospital day, was followed by two severe paroxysms of chills and a rise in rectal temperature to 106° F. A blood count revealed 42,100 leucocytes per cubic millimeter with 84 per cent neutrophiles (promyelocytes 1 per cent, myelocytes 2 per cent, metamyelocytes 10 per cent, band forms 41 per cent, segmented forms 30 per cent), 9 per cent lymphocytes (atypical 4 per cent, typical 5 per cent), and 7 per cent monocytes (atypical 2 per cent, typical 5 per cent). The blood smears showed moderate anisocytosis with tendency to microcytosis and active erythropoiesis as manifested by polychromatophilia and an occasional normoblast. Neutrophilic leucocytosis, with marked toxic granulation and toxic changes in the nuclei of segmented neutrophiles, was noted. There was marked left shift with immaturity to the

Fig. 2.—Eighth day. Hemorrhagic skin lesions covered with dry crusts.

leucoblasts. Toxic changes were noted in the monocytes and lymphocytes. The platelets were normal in number, appearance, and clumping. The blood picture was considered that of a leucemoid reaction. Streptomycin was started three days later because of the fear of possible secondary infection of the extensive raw surfaces in the mouth, eyelids, and denuded areas on the trunk. Plasma, blood, and glucose in physiologic saline solution were administered parenterally.

Two days later there was less evidence of erythropoiesis, and only an occasional polychromatophilic erythrocyte was noted. Leucocytes were less toxic in appearance with a left shift to the myelocyte stage. Platelets were normal in number, appearance, and clumping. The total white cell count dropped to 27,500 cells per cubic millimeter of blood. Skin lesions had involuted further, but bleeding and crusting of the lips and eyelids persisted.

On the twenty-seventh hospital day the sites of the involuted skin lesions were evident only by residual pinkish yellow macules. The oral mucous membrane was covered with a dirty white slough which bled readily when the child cried. The eyelids continued to show some thin crusts, and there was some whitish yellow, stringy exudate over the palpebral conjunctivae. The corneas were clear and uninvolved. Slight entropion of the left lower lid was evident.

The patient was discharged May 8, 1947, thirty-eight days after admission. At this time the cutaneous and mucous membrane lesions had completely healed. The only sequelae were slight conjunctivitis with minimal entropion of the left lower lid, and photophobia. Pigmented macules persisted at the sites of the former eruptions. Total serum protein concentration on the day of discharge was 7.92 Gm. per cent; serum albumin was 5.64 and globulin 2.28 Gm. per cent. Fasting blood sugar was 96 and blood urea nitrogen 10 mg. per cent. Serologic tests for syphilis were negative, and x-ray studies of the lungs and long bones revealed normal findings. Examination of the spinal fluid disclosed one cell per cubic millimeter, protein concentration of 22 mg. per cent, sugar of 60 mg. per cent, and chlorides of 668 mg. per cent.

Virus studies by the Virus Diagnostic Research Laboratory of the Children's Hospital of Philadelphia was reported by Dr. M. Michael Sigel as follows: "Spinal fluid, bulla fluid, mouth swabs and vaginal swabs collected on April 2, 1947, were examined for the presence of herpes simplex virus and vaccinia virus by inoculation into embryonated hens' eggs and on the rabbit cornea. All tests were negative.

RESULTS OF NEUTRALIZATION TESTS

DATE	INTERVAL AFTER ONSET	VACCINIA	HERPES SIMPLEX
April 24	25 days	1:16	1:64
May 7	38 days	1:256	1:64
July 3	3 months		1:16

"The presence of herpes neutralizing antibodies indicates either present or past infection, but does not establish which, because the first serum was obtained twenty-five days after the onset of illness; however, the failure to isolate herpes virus from numerous specimens taken earlier, strongly suggests that these antibodies were due to a long past infection. The rise in vaccinia-neutralizing antibodies between the twenty-fifth and thirty-eighth days of convalescence could be due to an anamnestic reaction or to a late secondary vaccinia infection of the eroded skin or mucous membrane. Again, the failure to isolate the virus practically eliminates vaccinia as the primary etiological agent."

Two months after discharge the child was active and well. There was a residual mild conjunctivitis and numerous deeply pigmented macules over the site of the former lesions. The entropion had almost completely disappeared.

On July 13, 1947, approximately four months after the onset of the episode which necessitated hospitalization, the child developed a rectal temperature of 101° F., irritability, redness and swelling of the gums and lips. Three days later she was afebrile, and her gums had become slightly hemorrhagic. Two days later the gums, the floor of the mouth, and the labial mucosa were almost completely covered with a gray slough. The eyelids became swollen and thick; yellowish material oozed from the eyes. The skin was not involved. Treatment consisted of hourly swabbing of the mouth with hydrogen peroxide and the instillation of penicillin ointment into the eyes every two hours. Eight days after the onset the gums had healed, the corneas were clear, and the patient was in good condition.

Examination on Oct. 22, 1947 was negative save for slight photophobia and pigmented skin residua.

DISCUSSION

Erythema multiforme with pluriorificial lesions affects males five times as often as females. It occurs most commonly in the spring and fall. Various agents, physical, bacterial, viral, antigen-antibody reactions, and drugs have been incriminated. As yet, no single specific etiological agent has been found. Blood cultures have been reported to be sterile by some authors. Results of eye cultures have been variable. It is likely that bacterial infection when present is due to secondary invasion. Extensive viral investigations,[3] employing blood, throat washings, and vesicle fluid in a variety of animals in addition to embryonic hens' eggs, have led to negative results. Histologic studies have been negative for inclusion bodies.

The Commission on Acute Respiratory Diseases[3] felt that their studies adequately eliminated as etiological agents the viruses of herpes simplex, vesicular stomatitis, and members of the psittacosis meningopneumonitis group in the material tested. In our case the rise of vaccinia-neutralizing antibodies between twenty-five and thirty-eight days after the onset of symptoms indicates either an anamnestic reaction or a late secondary vaccinia infection of the eroded skin or mucous membranes. The failure to isolate the vaccinia virus can be considered to preclude vaccinia virus as the primary etiological agent. The failure to isolate the herpes simplex virus from specimens taken early in the disease and the presence of herpes-neutralizing antibodies in serum taken twenty-five days after onset of the disease suggest a past infection with herpes simplex virus rather than one concerned with the patient's recent illness.

Drug idiosyncrasies (phenobarbital, nirvanol, Dilantin, phenolphthalein, sulfonamides) have not usually been directly concerned in producing the syndrome. One case resulted when an attempt was made to desensitize a patient who had a strongly positive reaction to an intradermal injection of caseinogen.[2] It has been claimed to be manifested occasionally after smallpox vaccination. It is quite possible that the various gradations of erythema multiforme are expressions of antigen-antibody reactions, depending on alterations, both quantitative and qualitative, in tissue or blood protein components. No definitive explanation can be given for the recurrence of mucous membrane lesions.

Studies of blood morphology have not revealed any consistent abnormalities. Anemia when present is probably an expression of the degree of bleeding, the nutritional status of the patient, and the extent of secondary infection. Both leucocytosis and leucopenia have been reported. A leucemoid reaction in our patient, following a sudden rise of temperature with chills and negative blood culture, could be explained on the basis of a pyrogen reaction. Thrombocytopenia has been noted[9] and may be related to the purpuric character of the lesions. The platelets were normal in the case herein reported. In another reported case a persistent eosinophilia (15 per cent) was noted.[4] Various blood chemistry determinations in a small number of reported cases were not abnormal.

Treatment before the advent of sulfonamides and antibiotics was mainly palliative and supportive, being aimed chiefly at maintenance of fluid and electrolyte balance and the prevention of sepsis and other complications. The local and intramuscular use of penicillin and streptomycin and sulfonamides administered orally has greatly simplified the control of infection and sequelae.

CONCLUSION AND SUMMARY

1. A case of erythema multiforme with pluriorificial lesions and recurrence of mucous membrane lesions is herein reported.

2. An etiological agent was sought by cultural methods and viral studies but not found.

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Medical Care

A THERAPEUTIC REGIMEN FOR ACUTE RHEUMATIC HEART DISEASE IN CHILDREN

LEO M. TARAN, M.D.
NEW YORK, N. Y.

THE evaluation of a therapeutic regimen for a protracted illness is one of the most difficult tasks in medicine when the proposed therapeutic program is based upon "nonspecific" forms of therapy. Recovery resulting from a form of therapy in such instances may mean complete recovery from the disease, symptomatic relief, or modification of the disease in favor of a more complete recovery. In the case of rheumatic heart disease, for example, recovery may mean complete cessation of rheumatic symptoms, actual interruption of the activity of the disease, or prevention of progressive cardiac damage while rheumatic activity runs its natural course. In proposing such a program it is necessary also to present evidence to show that this therapeutic plan is significantly more effective than no therapy at all or than other forms of therapy given adequate trial. In addition, it is mandatory to show that the particular therapeutic regimen does not produce any untoward effects either in the immediate present or in the distant future.

It is the purpose of this paper to present a therapeutic regimen for acute rheumatic heart disease in children. The forms of therapy proposed are well known; the method and the timing of their application are in some respects new and have been evolved over a ten-year period of intensive experience with rheumatic children observed under adequately controlled conditions.

A large number of rheumatic children (774) 6 to 16 years of age were observed during an episode of acute rheumatic heart disease. The therapeutic program was planned in advance ten years ago and was based upon two generally accepted premises: (1) The duration of rheumatic activity cannot, with our present methods of treatment, be modified, once the disease has passed beyond the stage of invasion. Failure to recognize and adequately treat the disease at the onset of the explosive or exudative phase seems to preclude the possibility of shortening the course of the subclinical or smoldering phase. (2) Acute rheumatic heart disease does not occur in the absence of rheumatic activity; progressive functional disability of the rheumatic heart occurs during rheumatic activity and not during quiescence; and progressive cardiac enlargement is a manifestation of rheumatic activity.

Criteria for the evaluation of the therapeutic results were established and rigidly followed. The type, dosage, and method of application of the thera-

From the St. Francis Sanatorium for Cardiac Children, Roslyn, Long Island, N. Y.

peutic agents were uniformly adhered to and deviations were made only to admit into our program the use of newer forms of therapy as they occurred over the years.

During the first five years of this study, the therapeutic program followed closely the commonly suggested forms of therapy (as to dose and method of application) for the various manifestations of acute rheumatic heart disease. (1) Salicylates were used when the patient showed obvious manifestations of rheumatic activity. (2) Digitalis was used whenever congestive heart failure manifested itself. (3) Mercupurin was used to increase diuresis when the manifestations of failure were moderate. (4) Oxygen was used only in patients who demonstrated severe respiratory distress.* Little attention was given to dietary regime or fluid intake. In general the patients were receiving a wholesome diet but no restrictions were made in the intake of salt. On the other hand, all of these patients were kept in a good physical and emotional environment. They were all treated in a sanatorium.

During the second five years of this study, a "specific" regimen was adhered to. Definite criteria were established as to when each one of these thera-

TABLE I. FORMS OF THERAPY (SECOND FIVE-YEAR PERIOD)

		SALICYLATES	DIGITALIS	MERCURIALS	OXYGEN	DEXTROSE + O_2 + INSULIN
Form		Sodium salicylates	Digitoxin	Mercupurin or mercuhydrin	Chamber B.P.—Normal T-66°, CO_2 1.3%	Dextrose—25-50% Oxygen— Chamber Insulin— Usual
Method		q2h day and night	Single or divided	Single—daily	Continuous	Continuous or interrupted
Route		Oral	Oral	Intramuscular	Respiratory tract	Dextrose—intravenous Insulin-subcutaneous
Dosage	Total	Bl. level 35-45 mgm. Vol. %	Ecg-Digit. effect	1-2 cc.	45-50%	25 gm. dextrose + 6 units insulin daily
	Initial	1½ grains/lb. body wt.	1-12 mgm./24 hours	½-1 cc./day	Same	Oxygen 45-50% (continuous)
	Maint.	Varies	0.1-0.2 mgm./day	Maint. "dry wt."	Same	Same
Duration		6-10 weeks	Varies	End of carditis	End of carditis?	1. Decrease in toxicity 2. Diuresis (3-6 wks.)
Additional medication	Bicarb. Vit. K Vit. C	Optional 1-3 mgm./day 100-300 mgm./day				
	Chlorides			Optional 45-60 grs.		
Reason for interruption		Severe salicylism (hyperventilation)	Toxic tachycardia, arrhythmias	"Allergy" (vaso-motor); dehydration	"Rheumatic Bronchitis"; manifest. failure	Increase in edema
Effective result		Laboratory and clinical evidence of carditis subsides	Subjective and objective evidence of failure subsides	Attainment and maintenance of "dry weight"	Laboratory and clinical evidence of carditis subsides	Subjective and objective Evidence of failure Subsides

*There was no consistent policy established as to when the above-mentioned therapeutic agents were indicated and when they were to be interrupted.

peutic agents were to be used, how long they were to be continued, and under what conditions they were to be administered. (See Table I.) The therapeutic results obtained in the group of patients treated in the first five years were compared with those obtained during the second five years.

CLASSIFICATION OF ACUTE RHEUMATIC HEART DISEASE

At the very inception of this study, it became obvious that acute rheumatic heart disease cannot be treated as a single entity. It became clear that this phase of rheumatic disease consists of various stages which are distinct in their manifestations and usually follow each other in sequence. It was noted that the disease falls broadly into two main categories: the stage during which the heart is actively disturbed but does not show any evidence of depletion of cardiac reserve; and the phase of obvious congestive heart failure. (See Chart 1.)

MANIFESTATIONS		Cardiac Functional Disability		Congestive Heart Failure			
		Stage of Invasion	Smouldering Phase	Left Heart Failure	Right Heart Failure	Left & Right Heart Failure	"Irreversible" Heart Failure
Toxic	Fever, Pallor	▲	Δ				▲
	Weakness, Cold and Clammy Skin	▲					▲
	Anorexia, Vomiting	▲					▲
	Anxiety, Restlessness	▲		Δ		Δ	▲
	Other Rheum Manif - Muscle, Joint, Skin	▲	Δ				Δ
Cardio-vascular	Heart Rate - (Tachycardia)	▲	▲	Δ	Δ	Δ	▲
	Fatigability	Δ	▲	▲	Δ	Δ	▲
	Angina		Δ	▲		▲	▲
	Dyspnoea and or Orthopnoea			▲		▲	▲
	Abdominal and G.I. Symptoms				▲	Δ	▲
	Dependent Edema				▲	▲	▲
	Labile Pulse	Δ	▲	▲	Δ	▲	▲
	Rhythm Disturbance (crude)	Δ		Δ	Δ	Δ	▲
	Blood Pressure	Decrease	Rise	No change	No change	No change	Rise
	Vital Capacity (decrease)		2+	4+	1+	2+	4+
	Ventilation (increase)		1+	4+	1+	2+	4+
	Venous Pressure (increase)				4+	2+	4+
	Circulation Time (increase)		2+	1+	2+	2+	4+
	Cardiac Enlargement		1+	1+	2+	2+	4+
Laboratory	Elevated ESR; Increased WBC; Depressed RBC and Hb.	▲	Δ	Δ			
ECG	Conduction Disturbance A-V	▲	Δ				Δ
	Prolonged QTc	▲	▲	▲	▲	▲	▲
	Local Tissue Anoxia - ST	Δ	▲				Δ
	Myocardial Disturbance - T			▲	▲	▲	▲
	Ventricular Strain - Left or Right					▲	▲
	Disturbance in Rhythm						▲

▲ Usual
Δ Occasional
1+ Slight
2+ Moderate
4+ Marked

Chart 1.—This chart shows the usual manifestations observed in most of the cases during each one of the phases of acute rheumatic heart disease.

I. CARDIAC FUNCTIONAL DISTURBANCE

Most patients at the onset of acute rheumatic heart disease show unequivocal evidence of cardiac disturbance without signs or symptoms of congestive failure. A marked tachycardia, easy fatigability, slight dyspnea on exertion, changing heart sounds and murmurs, and electrocardiographic alterations are observed much in advance of the classical signs of congestive heart failure. This

phase of the disease known as carditis is the most common single manifestation of rheumatic disease in children and may have a duration of three months to several years. It may be acute or smoldering. The degree of carditis may fluctuate from minimal to severe, leading rapidly to the second phase, namely, congestive heart failure.

A. The Stage of Invasion.—At the onset of carditis, the acute phase is dominated by the usual toxic manifestations of rheumatic fever. The patient has fever, is extremely pale, complains of weakness, marked perspiration, and cold and clammy skin. There is a high degree of emotional disturbance such as anxiety, restlessness, capricious appetite, irritability, etc. The child is likely to show other rheumatic manifestations in this phase of the disease. He usually presents arthritic manifestations, various skin manifestations such as erythema marginatum, etc. The usual laboratory tests such as the erythrocyte sedimentation rate, white blood count, hemoglobin determination—tests which are thought to be contributory to the diagnosis of rheumatic fever—are in most instances found to be positive in this stage of the disease.

On the cardiovascular side, there are few obvious findings. The child has a tachycardia; complains occasionally of fatigability; and has a slight decline in systolic pressure. There is no change in the circulation time and no increase in venous pressure. The heart does not show progressive cardiac enlargement on repeated examinations. On the other hand, nine out of every ten patients show a disturbance in conduction time on the electrocardiogram and all patients in this group show a very definite prolongation of the systolic time on the electrocardiogram.

While, therefore, the stage of invasion presents the usual "classical" manifestations of rheumatic fever, there is at the same time clear clinical and electrocardiographic evidence of mild cardiac disturbance.

B. The Smoldering Phase.—Once the acute toxic phase is passed, the patient settles down to a long drawn out, usually low-grade carditis. During this period very few of the toxic manifestations are present. The child usually has a normal temperature. The pallor is greater than the hemoglobin would warrant but is not as intense as in the stage of invasion. The diagnosis is often uncertain since the usual laboratory tests may be completely normal and may continue to be normal for many months while the activity of the disease continues. On the other hand, more definite manifestations of cardiac functional disability begin to accrue. The heart presents a tumultuous cardiac rhythm with a sinus tachycardia. The child occasionally complains of anginal pain and easy fatigability. On examination, the pulse rate is found to be labile. The blood pressure is usually higher than would be expected for the age of the child. There is a moderate decrease in vital capacity and an increase in respiratory rate as well as in ventilation. Repeated roentgen examinations show progressive cardiac enlargement. The electrocardiogram always shows a marked disturbance in the relationship between electrical systole and diastole. As has been pointed out elsewhere,[1] the Q-T interval is always markedly prolonged. The diastolic period is, therefore, very much shortened. The heart works under a false economy

of a prolonged contraction time impaired by a markedly shortened relaxation time. In most instances, when this sequence of events continues unabated, the electrocardiogram begins to show signs of local tissue anoxia. There are, however, no obvious signs of depletion of the cardiac reserve. There is no dyspnea or orthopnea. The venous pressure is normal and the blood velocity is within normal limits.

It would seem, therefore, that during the smoldering phase of carditis, the patient shows some adaptation to the disease process. He no longer shows clinically the toxic effects of the disease. On the other hand, he shows very definite disturbance in cardiac function as measured by some cardiac symptoms and evidence of disturbance in the integrity of the heart muscle on the electrocardiogram. There are no obvious signs of failure.

This phase of the disease may go on for months without entering the phase of failure. The greatest majority of patients do not show failure until a much later stage. A large number of these patients do not escape cardiac failure unless appropriate therapy is carried out.

II. CONGESTIVE HEART FAILURE

The average child with rheumatic heart disease does not show congestive failure unless a long period of carditis has preceded. This, of course, excludes the few rare occasions of a fulminating type of pancarditis. It has been observed that in children the earliest manifestation of heart failure concerns the left side.

1. Left Heart Failure.—At this stage, many symptoms of cardiac involvement manifest themselves. There is easy fatigability. There are frequent attacks of angina. There are various degrees of dyspnea or orthopnea. Upon examination, while the toxic manifestations of rheumatic fever are not prominent, there are undoubted signs of acute carditis present. The pulse rate is labile. There are occasional disturbances in rhythm, and from time to time a distinct gallop rhythm is heard. There is usually a marked decrease in the vital capacity and the ventilation is markedly increased. The blood circulation time is occasionally prolonged, although the venous pressure in most instances is normal. The heart is always found to be enlarged. The electrocardiogram shows the ever present disturbance in the systolic-diastolic relationship as well as distinct evidence of myocardial disturbance. T-wave changes in the limb as well as in the precordial leads are a frequent finding.

The degree of left heart failure may vary from that of minimal signs of respiratory distress to frank pulmonary edema and this may occur in the absence of any obvious signs of right heart failure.

2. Right Heart Failure.—Pure right heart failure is rarely seen in rheumatic heart disease in children. When it does occur, it is rather striking in that the child shows an enlarged liver, edema, and occasionally, facial edema without any signs of respiratory distress. The majority of patients do not demonstrate any toxic manifestations of rheumatic disease. The laboratory tests are usually normal for acute infection but many signs and symptoms of cardiac

failure are present. In this phase, the gastrointestinal symptoms are more likely to dominate the scene. There is nausea, vomiting, disturbances in evacuation, frequent upper abdominal pain, and distention.

The pulse rate is found to be labile. The blood pressure is normal and there is only a slight increase in ventilation. The vital capacity may be decreased only slightly. The venous pressure is raised and the blood circulation time is delayed. The heart is moderately enlarged. The electrocardiogram shows the usual disturbance of the relationship of systole to diastole and evidence of myocardial damage particularly as manifested by changes in the T wave.

In our experience, when right heart failure remains unabated for some time, the next phase of cardiac failure is inevitable.

3. Left and Right Heart Failure.—At this stage there are few manifestations of the toxic rheumatic disease. There are, frequently, complaints of precordial pain often typically anginal in character. At other times, the precordial distress is of an indefinite nature; diffuse precordial annoyance and a feeling of constriction. The patient shows the manifestations of respiratory distress as well as the manifestations of right heart failure. There is dyspnea and orthopnea. There are occasional gastrointestinal symptoms. The venous pressure is raised and the circulation time is delayed. The vital capacity is low and the ventilation is high. The heart becomes markedly enlarged. At this stage, the usual electrocardiographic findings are those of ventricular strain either right or left. In addition, the patient continues to show clinical evidence of carditis. The pulse is labile, the heart is tumultuous, and there is frequently a marked gallop rhythm. There are occasional crude disturbances in rhythm in addition to a marked tachycardia.

Many of these conditions, as will be shown later, are reparable and the patients return to a relatively good state of cardiac reserve. Some progress to the "irreversible" stage.

4. "Irreversible" Stage.—At this phase, there is a distinct and rather dramatic return of all the toxic manifestations of rheumatic disease. There is low-grade, fluctuating fever and marked pallor. The patient once again complains of extreme weakness, cold sweats, and a cold, clammy skin, and shows marked anxiety and restlessness. There is a recrudescence of joint swellings with many bizarre rheumatic skin manifestations, a marked tachycardia, and extreme cardiac fatigue. The patient often has acute attacks of angina. Some of these attacks are long lasting and difficult to control with sedation. There is marked dyspnea and orthopnea. The liver is markedly enlarged. The upper abdomen is tender, and there is usually a high degree of edema and ascites. Most patients in this stage show a considerable rise in systolic blood pressure; a marked rise in venous pressure and a great delay in circulation time; a marked depression in vital capacity and a marked increase in ventilation sometimes reaching as much as ten liters per minute per square meter of body surface. The heart is markedly enlarged. The electrocardiogram in this stage may show any or all of the abnormalities mentioned previously. Many patients also show crude disturbance in rhythm such as auricular fibrillation, premature

ventricular contractions, etc. All patients show a marked prolongation of the systolic period on the electrocardiogram and a relatively marked shortening of the diastolic period.

It is noteworthy that in spite of the high degree of failure, many cases show positive laboratory evidence of active infection such as an elevated erythrocyte sedimentation rate, an elevated white blood count, and a marked depression in the hemoglobin.

In summary, it might be said that there are six distinct stages in the evolution of acute rheumatic heart disease leading to "irreversible" failure. The first is the stage of invasion where the picture is dominated by the toxic manifestations of acute rheumatic fever. Few if any symptoms of heart disease are present and the earliest inkling that the heart is involved is expressed in disturbances in conduction time on the electrocardiogram. The next four stages no longer demonstrate the toxic manifestations of rheumatic disease but show more evidence of cardiac disability as the disease progresses from the smoldering phase to the phase of left and right heart failure. And finally, there is the "irreversible" stage of heart failure where the degree of activity of the disease is once again at a high level and the degree of severity of heart failure is markedly increased.

It may be noted that the only feature which is present in all these phases and which in our opinion demonstrates the presence of active carditis is the disturbance in the systolic-diastolic relationship of the cardiac function: systole is prolonged and diastole markedly shortened.

THERAPEUTIC MEASURES (CHART 2)

In the planning of any therapeutic regimen, it is customary to consider the following therapeutic measures:

A. The external environment under which the patient is being treated.
B. The internal environment which is provided for him in terms of nutrition.
C. The specific or supportive medication.

A. The Environment Under Which the Patient Is Being Treated.—It has long been recognized that for a patient suffering from heart disease, complete rest is needed first and foremost. In recent years more stress has been placed upon emotional rest rather than physical rest. In some quarters, the pendulum is swinging away from restricted bed rest to avoid complications which are inherent in prolonged rest.[2]

Experience with acute rheumatic heart disease teaches two lessons in this respect: (1) Physical rest continues to be a most essential part of the treatment as long as rheumatic activity in the heart muscle is present. Failure to attain a good measure of physical rest interferes with all other forms of therapy. Experience has also shown that an increase in physical activity during the phase of active rheumatic disease encourages progressive cardiac damage during that phase of the disease. It has become perfectly obvious that unless an

environment is created whereby the child has complete emotional rest in the form of security and a certain measure of contentment and happiness, the necessary degree of cardiac rest cannot be attained. It is for this reason that sanatorium care[3] is suggested. It is also for this reason, in our opinion, that results attained at the sanatorium compare most favorably with results attained elsewhere.

THERAPY		Cardiac Functional Disability		Congestive Heart Failure			
		Stage of Invasion	Smouldering Phase	Left Heart Failure	Right Heart Failure	Left & Right Heart Failure	"Irreversible" Heart Failure
Cardiac Rest (Physical and Emotional)		+	+	+	+	+	+
Dietary Regimen	High Protein	+	+	+	+		
	High Vitamin	+	+	+	+	+	+
	Na Poor			+	+		
	Na Free					+	+
	Cl Increase			+	+	+	+
	Fluid (amt.)	normal	normal	increased	increased	2-3 qts./day	Limited
"Specific" Medication	Salicylates	●	□	□	□	□	□
	Digitalis	•	•	•	○	?	•
	Mercurials	?	?	●	○	●	●
	Digitalis + Merc.	•	•	•	●	○	□
	Oxygen	○	●	?	□	?	□
	Dext + O_2 + Insulin	?	□	□	?	?	●

● Most Effective □ Ineffective
○ Effective • Contraindicated
? Questionable Value + Indicated

Chart 2.—This chart shows the therapeutic regimen that was followed during the second five-year period.

B. Nutritional Requirements.—The influence of diet upon the progress of rheumatic heart disease has been discussed for many years. The pendulum has swung from limited Karrel type of diets to high calorie, high protein, high vitamin diets. Our experience shows that during the stage of invasion and the phase of protracted carditis as well as early cardiac failure, a high protein high vitamin diet seems to produce more favorable results than diets poor in sodium and limited in calories. When the patient has reached the stage of both left and right heart failure, it would seem that the best results are attained by putting the patient on a sodium poor diet in the form of a modified Karrel diet. The routine has been to place the patient on one to one and one-half quarts of milk daily or about 1 to 3 Gm. of sodium daily. When the patient has reached the "irreversible" phase, this diet becomes mandatory if any results are to be attained.

The fluid intake during the first two phases of acute rheumatic heart disease need not be modified. Once the cardiac reserve is impaired, it would seem that the fluid intake must be increased, and when the patient has reached the phase when he has both left and right heart failure, a regimented effort must be

made to increase the fluid intake to between two and three quarts daily. This increase in fluid, however, cannot be continued once the patient has entered the "irreversible" phase. At this phase the fluid intake must be sharply limited. The reason for this is not at all clear.

To summarize, our nutritional regimen is predicated upon the following principles: (1) During the stages of invasion and functional cardiac disability when the cardiac reserve presumably is normal, the patient should be kept on a high protein, high vitamin diet with a normal amount of fluid and salt intake; (2) Once the patient enters the phase of decrease in cardiac reserve, a modification of the diet is an important part of the program depending upon the degree of decrease in cardiac reserve. The more the cardiac reserve is depleted as expressed by the degree of cardiac failure, the more limited does the diet have to be principally for the purpose of decreasing the salt intake, and the larger does the fluid intake have to be to attain satisfactory diuresis. The exceptions to this rule are the patients in whom the cardiac reserve is very low and the element of rheumatic activity high. In these instances, the patient does not seem to be able to excrete the sodium but at the same time cannot tolerate even a normal amount of fluid intake.

C. "Specific" or Supportive Medication.—In the treatment of acute rheumatic heart disease many forms of therapy have been used. Salicylates, digitalis, mercurials, oxygen, concentrated glucose, all have been used from time to time. The reported results with these various forms of therapy range from complete disappointment to a high degree of enthusiasm. From our point of view, the reason for such a discrepancy in reported results is not the form of therapy but the choice of patients to whom it was administered.

1. Salicylates: In our experience, salicylates in large doses may be considered in the nature of a specific therapy if given to the patient during the stage of invasion. Thus, when a patient suffers from an acute carditis in the exudative stage, particularly during the first six weeks after the onset, large doses of salicylates more often than not (80 per cent of the cases) interrupt the onslaught of the illness. All clinical and laboratory evidence of activity subsides and the patient makes a complete recovery, often within a period of a few weeks. The results in these cases are not unlike those seen in instances of acute polyarthritis. Our experience teaches that eight out of every ten patients, if treated at this time with sufficient salicylates to raise the salicylate level to between 350 and 450 micrograms, can be saved from the next phase of the disease, namely, the smoldering type of carditis.

In addition, there is solid evidence to show that salicylates in sufficient dosage make no impression upon the course and the outcome of acute rheumatic heart disease if they are administered after the stage of invasion. Briefly, therefore, proper salicylate therapy is an important form of treatment if applied at the proper phase of the disease.

2. Digitalis: It has repeatedly been stated that the so-called "specific" drug for heart disease has been losing ground in its importance particularly in the treatment of acute rheumatic heart disease.[4a, b, c, 5, 6, 7] For many years we have

been impressed with the fact that the ill effects of the proper use of digitalis in acute rheumatic heart disease outweigh any possible beneficial effects. In our experience, there is no stage in the disease where digitalis alone can be said to be most effective. On the other hand, there are many stages in the disease during which the use of digitalis produces incontrovertible evidence that more harm is done by the use of the drug than by withholding it. It is generally agreed that patients with acute hearts may be more sensitive to the usual doses of digitalis. On this account, a careful plan has been followed in the use of digitalis in acute rheumatic heart disease. In all cases concentrated digitalis preparations are used controlled by repeated cardiographic tracings to gage full dosage as well as toxic effects. Enough evidence has accrued to show that during the stage of invasion and the stage that follows, namely, the stage of functional disability of the heart, as well as during the stages of left heart failure and so-called "irreversible" heart failure, proper use of digitalis produces toxic effects much before any therapeutic effects are observed. In many cases these toxic effects with doses too small to expect any therapeutic effects range from premature contractions to toxic rhythms, and all types of arrhythmias. Occasionally, in instances of right heart failure digitalis seems to be effective when used alone.

Briefly, the use of digitalis in acute rheumatic heart disease is of limited value. In our experience, it would seem that one might well do without the use of this drug in the vast majority of instances. The possible exception to the rule would be in auricular fibrillation with a fast ventricular rate. Even in these cases when the arrhythmia occurs during the so-called "irreversible" phase or during the phase of "pure" left heart failure, the usual effect of digitalization upon auricular fibrillation is not attained in the average case.

3. Mercurials: Our experience coincides with the experience of other observers that when mercurials are properly used, they take the place of digitalis in acute heart disease. During the first two phases of acute heart disease it is of questionable value. The patients showing symptoms of left heart failure can be treated most effectively with the use of mercurials. Frequent small doses given intramuscularly must be continued until dry weight is attained and from then on the patient is placed on a maintenance dose of Mercupurin or Mercuhydrin until all evidence of acute heart disease has subsided. It is important to remember that mercurials are continued not only until evidence of congestive failure has subsided, but until all evidence of rheumatic activity is no longer present. This form of therapy may have to be continued for many months.

There are no contraindications to the use of mercurials if they are used judiciously. It is widely agreed that mercurials should be used intramuscularly rather than intravenously as the occasional fatality that occurs as a result of mercurial injection is limited to the patients who received the medication intravenously. Furthermore, the effect in our group of patients can be produced equally well with the intramuscular route. Occasionally (1 in 200 patients) a child will show what seems to be an allergic response to a certain form of

mercurial diuretic. This allergic response is expressed usually in the form of a vasomotor collapse ranging in severity from mild and transitory to severe, necessitating emergency cardiac therapy. When such response occurs with Mercupurin, Mercuhydrin does not produce the same response, and vice versa. The nature of this sensitivity is not clear. Some children develop signs of severe dehydration but this can be avoided by giving ample amounts of fluids during the course of the mercurial therapy.

4. Oxygen Therapy: The routine use of oxygen therapy in acute heart disease has not been proposed definitely heretofore. The method which we employ and the results which we attain thereby have been described elsewhere.[8] The routine is as follows: The patient is placed in an oxygen chamber containing 45 to 50 per cent oxygen and 1 to 1.5 per cent carbon dioxide. He is kept in the chamber until all clinical and laboratory evidence of carditis have subsided. The duration of this period may range from ten weeks to several months.

We have observed no beneficial effects from oxygen in cases of acute heart disease with heart failure. Furthermore, in the irreversible type of heart failure, oxygen therapy alone is definitely ineffective. In cases of left heart failure, it is of questionable value. This form of therapy, however, is of specific value in the smoldering type of carditis which demonstrates no depletion of cardiac reserve but shows all the evidence of impairment in the functional integrity of the heart. In these instances, the effect is striking and rapid. An analytic description of the value of this form of therapy for these cases has been presented elsewhere.[8] In our experience there are two definite contraindications to oxygen therapy in acute rheumatic heart disease in children. Patients who present evidence of bronchitis during the course of rheumatic activity should not be introduced into a high oxygen atmosphere. All of these patients develop severe symptoms of respiratory distress and must be removed almost immediately. The mechanism of this is not clear. The group of patients, as mentioned above, who manifest advanced heart failure do poorly in a high oxygen atmosphere.

5. Concentrated Glucose: The use of concentrated glucose in heart disease has been tried from time to time. In our experience, the cases of so-called "irreversible" heart failure where the toxic element of the disease is high and at the same time the cardiac reserve is extremely low, a few cases are definitely improved by the use of this form of therapy.

The patient is given intramuscularly 25 Gm. of dextrose daily. This is given in two doses of either 25 c.c. of a 50 per cent solution or 50 c.c. of a 25 per cent solution, one dose before breakfast and the second dose in the early evening. At the same time, the patient receives subcutaneously an injection of insulin equivalent to about one unit to every three or four grams of carbohydrate. In addition, the patient is given oxygen for one hour by mask or catheter following the injection of dextrose. This form of treatment is continued until all signs of toxicity subside and a well-established diuresis has been attained. The average patient needs approximately three to six weeks of this form of therapy. Once the patient shows the above-mentioned signs of improvement and is no longer considered as having the "irreversible" type of

heart failure, he is then treated with mercurials used in the method described above. The effectiveness of this type of therapy in the "irreversible" group of cases is questionable since only about one in ten patients seems to be relieved. In our experience, a great many patients early in the course of the treatment show failure to respond. The only contraindication to this form of therapy that we have observed is increasing dependent edema which seems to be definitely associated with the therapy rather than the course of the disease.

In summary, therefore, it may be said that while the types of medication administered in this regimen have been used from time to time, the method of application is new. Salicylates are an almost specific form of therapy when used during the stage of invasion. Oxygen therapy seems to belong in the same category if used in the stage of smoldering carditis without heart failure. Mercurial diuretics used in a specific way have displaced the use of digitalis in acute left heart failure. Digitalis finds limited use in acute rheumatic heart disease but may be tried in cases where the dominant feature is right heart failure. In the patients in whom the activity of rheumatic disease has depleted the cardiac reserve as manifested by both left and right failure, the use of mercurials in addition to digitalis seems to be the therapy of choice. The proposal to use concentrated glucose with oxygen and insulin is made with misgivings. It seems that a few of the so-called "irreversible" heart failure patients do well with this form of therapy.

RESULTS

In the past five years (1942-1947), 376 children with acute rheumatic heart disease were treated in the manner described above. These were carefully classified first as to the phase of acute rheumatic heart disease. They were then placed on the appropriate treatment as outlined. In the preceding five-year period (1937-1942) another group of 398 patients were also classified as to the phase of the disease that they presented but the treatment in this group was not systematic and did not follow any particular pattern. In most cases of the latter group, salicylates were used in all phases of the disease where a diagnosis of active rheumatic disease was made. The dose was insufficient in most cases and no attempt was made to gage the dose by determining the level of the salicylates in the blood; digitalis was used liberally; mercurials were used where evidence of heart failure was present but this was used in interrupted doses and results were judged by the amount of diuresis attained at the time. No attempt was made to determine a maintenance dose, and mercurial diuretics were stopped as soon as obvious evidence of failure subsided. Oxygen was used only as an emergency form of therapy. Patients were treated in oxygen tents or by catheter when severe signs of heart failure were present, particularly left heart failure. The use of glucose, oxygen, and insulin was attempted only as a form of emergency cardiac therapy.

When the two groups are compared, i.e., the group treated during the first five-year period and the group treated in the last five-year period, striking differences are observed. (See Chart 3, Table II.) Of the total number of 398

patients treated in the first five-year period, about 25 per cent made a recovery from the attack for which they were treated. In the group of patients treated in the last five years, the recovery rate was more than twice as high (58.7 per cent). This difference becomes even more striking as we analyze the various

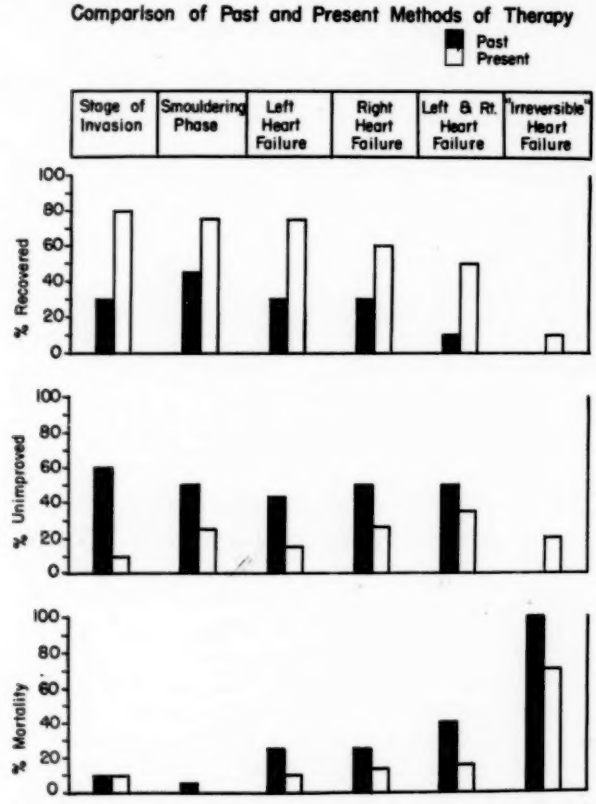

Chart 3.—This chart shows the percentage incidence of patients recovered, unimproved, and the mortality in each of the two five-year periods.

TABLE II. COMPARISON OF PAST AND PRESENT METHODS OF THERAPY

	NUMBER OF PATIENTS		RESULTS					
			% RECOVERED		% UNIMPROVED		% MORTALITY	
	PAST	PRESENT	PAST	PRESENT	PAST	PRESENT	PAST	PRESENT
Stage of invasion	60	50	30	80	60	10	10	10
Smoldering phase	50	40	46	75	50	25	4	0
Left heart failure	68	60	31	75	45	15	24	10
Right heart failure	100	130	30	60	50	27	20	13
Left and right heart failure	80	66	10	50	50	35	40	15
"Irreversible" failure	40	30	0	10	—	20	100	70
Totals	398	376	25.1	58.7	45.7	22.3	29.1	11.1

phases of acute heart disease. In the stage of invasion and in the smoldering phase, eight out of every ten patients recover from the acute attack if given the proposed form of therapy, whereas formerly the recovery rate was from 30 to 46 per cent. Of the patients who show a depletion of cardiac reserve, the recovery rate is more than twice as great with the present form of therapy as with that used in the past. In the group with left heart failure, three out of every four patients recovered from the acute attack; of those with right-sided failure, three out of every five; in those with both left and right failure, one out of every two; and in the "irreversible" group, one out of every ten. The best results during the first five-year period were three out of every ten patients in any phase of congestive failure and in the "irreversible" group, none recovered.*

Of those children who did not recover in either of the two groups, some became progressively worse, graduating from a milder phase of acute heart disease to a more severe phase, and some died during the acute attack. Almost one-half of the patients treated in the first five-year period became progressively worse and practically one-third of the patients died during the acute attack. With the newer therapeutic regimen, only 22 per cent became progressively worse and a total of 11.1 per cent died during the acute attack. These results become more striking when one subdivides them according to the various phases of acute heart disease. In the stage of invasion, if the patient is treated inadequately, his chances of becoming progressively worse are about 60 per cent as compared with 10 per cent when treated adequately. In the smoldering phase, one out of every two patients becomes progressively worse with the old system of therapy as compared with one in every four when treated with the new regimen. In the group of patients with heart failure, one out of every two becomes progressively worse when inadequately treated, but when therapy is adequate, of the patients with left heart failure only one in six might become progressively worse and in right heart failure and in left and right heart failure from one-quarter to one-third of the patients become progressively worse.

In all the phases of acute heart disease, the mortality rate is much lower in the group which is adequately treated as compared with the group which is treated in the old manner. It is obvious that the mortality rate rises in both groups as the disease progresses from the early stage of invasion to the "irreversible" phase. But the mortality rate is significantly lower during the second five years of this study.

COMMENT

There is general agreement that the interest in the treatment of rheumatic fever and rheumatic heart disease has lagged behind when compared with the ever-increasing interest in the etiology and pathogenesis of this disease. The reason for this lag stems from the fact that the clinical concepts relative to the course and behavior of acute rheumatic disease have for many years been nebulous and confusing. Thus a therapeutic hopelessness has dominated the thinking as regards the treatment of this disease.

*That is where the name "irreversible" found its origin.

In recent years, it has become fairly clear that disability resulting from rheumatic heart disease is an expression of the acute inflammatory process in the heart muscle rather than the extent of valvular damage. This concept implies that the chemical or metabolic changes which take place during the acute phase of the disease contribute much more to the functional disability of the heart than does the mechanical impairment of the heart as a pump resulting from fibrosis of the valves. If, then, we adhere to this concept, it is obvious that the treatment of rheumatic heart disease during the acute phase is the primary aim in the management of the cardiac disability resulting from rheumatic disease. Our experience in this regard teaches the important lesson that the outlook for the patient with acute rheumatic heart disease is not hopeless but favorable indeed provided that the therapy is aimed at: (1) stopping the invasion of the heart muscle at the onset of rheumatic carditis; (2) relieving myocardial anoxia before heart failure has become manifest, and; (3) improving impaired cardiac function by relieving the signs of failure occurring during the acute phase of the disease.

We are impressed from the experience presented in this paper that a judicious, fearless, and patient use of salicylates distinctly delimits the invasion of the disease. Once the invasion has advanced unhindered, the duration of rheumatic activity cannot be shortened. At this stage of the disease, relieving the burden imposed upon the heart muscle by local tissue anoxia prevents, in a large majority of cases, cardiac disability as expressed in congestive heart failure. The treatment of these two phases of the disease, therefore, is of paramount importance and if carried out properly decreases the total cardiac damage resulting from rheumatic disease. Once the heart has begun to fail, dehydration therapy must be given to prevent further failure. This dehydration therapy can best be attained by adequate control of salt and fluid intake and by persistent and judicious use of mercurial diuretics.

It has been mentioned from time to time that digitalis therapy in acute rheumatic heart disease is of limited value. Our experience concurs with this observation. We are, on the other hand, impressed with the fact that digitalis in proper therapeutic dosage in acute rheumatic heart disease cases produces toxic digitalis effects much before any therapeutic effects may be obtained. It would seem that the patient with acute rheumatic heart disease shows a high degree of sensitivity to digitalis precluding its use to produce therapeutic effects. It is further clear that the more acute the carditis, the more precarious is the use of digitalis. We have not been convinced that the toxic effects of digitalis produced in acute rheumatic heart disease are a matter of improper dosage.

It is common experience that under the best of therapeutic conditions, many patients with acute rheumatic heart disease go downhill toward a catastrophic end. This group of patients, in our experience, seems to manifest an acute explosive recrudescense of rheumatic disease superimposed upon a heart whose reserve has already been markedly depleted. It would seem from the experience presented here that an attempt to improve cardiac nutrition may yet save a few of these individuals.

The methods of application and timing of the therapeutic measures discussed in this paper have been evolved in an environment which played an important role in producing the results noted above. It must be said that without the complete physical and emotional rest such as can be attained only in a sanatorium type of environment, the therapeutic effects would fall short in producing the favorable results presented. On the other hand, sanatorium environment alone without a systematic therapeutic regimen fails to effect the clinical course of the disease in a significant way. The primary aim in the treatment of acute rheumatic heart disease is the attainment of complete cardiac rest during the unfavorable circumstances imposed upon the heart by the presence of an acute inflammatory process in the heart muscle. Thus, when the period of invasion has proceeded unchecked, complete cardiac rest can be attained by relieving local tissue anoxia or by decreasing the burden imposed upon the heart by those dynamic factors which are responsible for cardiac failure.

CONCLUSIONS

1. A therapeutic regimen for the treatment of acute rheumatic heart disease in children is presented.

2. Acute rheumatic heart disease has been classified into six phases.

3. The stage of invasion can be treated most effectively with adequate salicylate therapy.

4. The stage of protracted carditis can be favorably influenced by adequate oxygen therapy.

5. The stage of heart failure is adequately treated with dehydration therapy attained by a regimented use of mercurials and salt and fluid intake.

6. Complete physical and emotional rest, best attained in a sanatorium type of environment, plays an important role in the proposed therapeutic program.

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Psychologic Aspects of Pediatrics

PHYSICAL ILLNESS AND CONVALESCENCE: THEIR MEANING TO THE CHILD

WILLIAM S. LANGFORD, M.D.
NEW YORK, N. Y.

IT IS the rare child who grows into maturity without having gone through one or more episodes of physical illness. Clinical psychiatric observations reveal that physical illness in a child, no matter how trivial, has its own unique meaning for the child and his parents and may be a focus out of which emerge emotional disturbances of far-reaching significance. Much can be done to make a child's illness an emotionally less traumatic and destructive event than it frequently is. Many things which happen to the sick child and contribute to current and future emotional disturbances are preventable if a little thought is taken and the child is looked on as a thinking, feeling, acting human being. If the physician is willing to go further and attempt to understand what illness itself may mean to the average child and what he feels about it, the emotional disturbances may be further minimized, and the total experience may be a constructive growth experience for the child.

When a child becomes ill many things happen to him which are strange and new and are poorly understood by him. He does not feel well, understands little of why he has become sick, is irritable, and perhaps wants to be left alone. His own anxiety is often intensified by that of his parents, who may become guilty and anxious about their own part in the production of the illness or their failure to have prevented it. The usual amount of parental concern and fussing may well be increased if the illness is not a clear-cut one. At such times the confusion of the child and his parents is then enhanced by the perplexity of the doctor.

When a child must be admitted to a hospital he has to face separation from his parents, his home, and all with which he is familiar and meet a new environment at a moment when he is handicapped by his illness, his confusion, and his anxiety. At such times even the most "normal" child is likely to want to cling to his parents, who are, after all, his natural pillars to lean on in times of stress. The more anxious and upset the parents are at these times, the more difficult it is for the child to separate himself from them.

Many children are brought to the physician poorly prepared for hospitalization, should it prove necessary. Often the parents assure the tense, anxious, ill child that he is going "just for an examination," only to have the plans changed by the physician who feels that hospitalization should take place. At these times the physician will often tell the mother that hospitalization is necessary and leave her entirely on her own to break the news to the child and to squirm out

From the Babies Hospital, New York, and the Departments of Pediatrics and Psychiatry, College of Physicians and Surgeons, Columbia University.

of the promises she had made as best she can. The child then feels that he has been betrayed and let down by someone on whom he should be able to rely; he is likely to look on his admission to the hospital as an abandonment by his parents. Some hospitals do not permit the parent to accompany the child to the ward, thereby increasing the feeling in the child that he has been left by those who should love him. If the physician on the ward is not the one who sees the child in the clinic, the child feels that no one in the hospital is familiar with him or his problems. In practice, when the mother is permitted to accompany the child to the ward and to talk to the nurse who will later have charge, the degree of separation anxiety in the child is lessened and his adjustment to ward routines is enhanced. The wise physician will try to ascertain what the child has been told of the reasons for coming to visit the doctor or for admission to the hospital.

Children are often exceedingly poorly prepared for routine visits to the physician and may be told fantastic tales as to why they are going to be admitted to the hospital. One boy with acute appendicitis was brought to the hospital in the middle of the night in his pajamas with his sled, having been told by the parents that he was going for a sleigh ride. It was several days before he could meet any of the hospital personnel without an attitude of complete suspicion. Another boy who had been told by his father that he was to have an enema and then go home, awoke from the Avertin anesthesia with a surgical dressing on his abdomen and refused to talk to his father during the rest of his stay in the hospital after greeting him initially with the remark, "Daddy, you are a liar."

If visiting hours are restricted it should be made clear to the child that the decision is one made for, not by, the parent. Parental visiting is often an upsetting event for the child and is regarded as necessary but bothersome by the hospital personnel. Troublesome parents may be discouraged from visiting; this procedure does not take into account the child's bewilderment as to why other parents visit but his do not.

ILLNESS AS PUNISHMENT

Although the meaning of a specific illness to a particular child depends upon a large number of factors in his past experience and on the attitudes of his parents, there are some things which are common to most children who become sick and which affect their attitudes and reactions toward the illness. To most children sickness comes as punishment for their misdeeds. In this belief children differ little from our ancestors only a few generations ago when sickness was regarded as punishment for the collective and individual sins of mankind. Beverly[1] reported in 1936 that 90 per cent of a group of children at the Children's Memorial Hospital in Chicago stated that they got sick because they were "bad"; eighteen out of twenty-one diabetic children said that they "ate too much sugar"; and 90 per cent of a cardiac group believed that they were ill because they "ran too much."

Similar ideas were garnered from children who were patients in the Babies Hospital. Almost all of the children seen a few years ago in a convalescent home for children with rheumatic heart disease subscribed to the belief that their illness was, at least in part, caused by disobedience of parental commands and

that their placement in a convalescent home had some of the elements of being sent away because they were bad; this was especially true in those who were making a poor adjustment to the convalescent placement. The change in the adjustment of these children when they were helped to see that their illness and placement away from home were not in the nature of punishment was rapid. Some children are a little sheepish in owning up to fears that the illness is punishment and reveal these fears only after seeking reassurance that they will not be laughed at. One of our patients who had had several admissions to various hospitals and convalescent homes because of recurrent attacks of rheumatic fever with carditis, adjusted poorly on each hospitalization and placement. At the time she was seen she was irritable and demanding of extra attention from the nurses, she resented any attention paid to the other children on the ward, and she was insistent that her mother bring her toys and books at each visiting hour. These she rarely looked at once she had them. When her illness was discussed with her she gave the following reasons as to why she had become sick: "If you run and jump your heart beats fast so you get sick"; "One time I went sleigh riding and it tips over so you get a cold"; "I didn't obey my mother"; "You don't obey your mother and run out—you run up and down stairs"; (quite sadly) "It's my own fault I get sick"; she added rather tentatively, that fighting and disobeying caused one relapse in her illness. At least part of her behavior toward the hospital personnel and her mother seemed to have as its goal making sure that she was not being further punished.

Parental admonitions intensify any latent fear that the child may have that his illness comes as a punishment. Colds come because the child disobeys and does not wear his rubbers. A leg is broken because the child does not heed his mother's cautionary advice not to roller skate in the street. Upset stomachs could be avoided if the child would only eat what he is supposed to. Eyes are ruined by reading fine print or reading in poor light or from too assiduous attention to the comics. The warnings about what will happen are often supplemented with an "I told you so" when something does happen to the child. These are common statements by almost all parents and contribute to the child's idea that when he is sick he is being punished. The all too common practice of threatening the child with the doctor or with an operation if he continues to be bad (which to many parents means disobedience) lends further reality to the child's fears when he becomes sick and he is taken for medical advice. We have observed several children with hematuria associated with acute nephritis who were sure that they had caused the damage through masturbation. Their anxiousness was intense and interfered not only with their adaptation to the hospital routines but with their capacity to participate in the therapeutic regimen laid down for them. We can feel sure that in most sick children there is a certain amount of anxiety because of their ideas as to the cause of their illness and in many guilty feelings as to their own responsibility.

REGRESSIVE REACTIONS

Most observers are aware of the frequency with which some degree of psychologic regression back to an earlier level of emotional and social adaptation

occurs as a part of the personality reaction to almost any illness. This takes place in adults as well as in children. Regression takes place in the child as a defense against his anxiety and is dependent on the severity of the emotional disturbance and the length of the illness. Liss[2] has pointed out that the more severe regressions back to an infantile preoccupation with purely physical functions of food intake, metabolism, and excretion occur in the more prolonged or traumatic illnesses. He believes that this phenomenon may well be a technique of self-preservation in which all of the resources of the organism are marshalled to preserve life and energies and are not dispersed into nonessential activities. There is at the same time a similar preoccupation on the part of the medical attendants of the sick child in the fluctuations of the body temperature, respiratory and pulse rates, appetite, intestinal and urinary tract function, and symptoms, which contributes to but does not seem responsible for the child's regression back to a physical self-absorption. The younger the child at the time of the illness the more quickly the regression occurs. In general, the most recently acquired behavior habits and social techniques are the first to go. Finally, all expression of social relationships leaves and all that is left is a rather primitive insistence on and interest in food and affection. Symptomatically, what we observe in many sick children is an expression of emotional and social needs and outlets appropriate to a younger age period. The lusty boy of 9 years or so who in normal circumstances would as soon be found dead as crying, and who when he does cry yells vigorously, may under the stress of illness begin to whimper and mewl in the manner of an infant. Along with this comes a desire for affection and cuddling even in the public atmosphere of the hospital ward. In some children we observe the dramatic emergence of such infantile symptoms as thumb sucking, a baby-talk kind of speech difficulty, and enuresis. Masturbation especially is likely to occur after operations. In some older children a hypochondriacal preoccupation with bodily symptoms and functions may be a prominent part of the picture.

In the usual illness which is relatively short-lived this is likely to be transitory in nature. In children with some illnesses such as ulcerative colitis the regression to a highly infantile, dependent emotional state occurs quite rapidly early in the course of the disease and is more marked than the severity or duration of the disease process would lead us to expect. Here the severity of the personality disturbance which accompanies the disease process seems related to the basic personality structure and functioning of the child and is only partly a result of the way in which a sick child is regarded and handled. We have observed regressive reactions in children with slowly growing brain tumors who were brought for medical advice because of the personality change.[3] None of these children with intracranial tumors was regarded by the family as having an organic illness at the time when they were brought for medical help. Euphoria, which is on occasion seen in adult patients with certain grave disease and which is usually regarded as having an ego protective function, is unusual in children in our experience.

CONSTRUCTIVE RESPONSES

Some children respond to difficult situations in a constructive manner; to them an illness may cause minimal emotional disturbance. In fact, to many children a period of illness, if well handled by the parents, nurses, and physicians involved, may result in a constructive growth experience. All who have observed a large number of sick children in the hospital or in the home are familiar with the child who develops constructive compensations and comes out more mature than he was before he was sick. In this group of emotionally stable and healthy children it is rare to see intense separation anxiety if hospitalization is necessary. The parent-child relationships to which such children have been exposed have been, for the most part, healthy ones, and the parent, when confronted with the necessity of hospitalization for the child, does not respond with overwhelming anxiety which is communicated to the child. In the hospital, especially during the brief convalescent period before the child goes home, he makes friendships with other children on the ward and with the nurses. These friendly relationships often last long after the child leaves the hospital and goes back to his usual activities. The child often collects autographs from the hospital personnel and other child patients. When he is well enough he enters into the activities and routines of the ward and helps the charge nurse in various ways.

The convalescence of this group of children is a relatively easy one to supervise. Some of the younger children are able to work off some of the more normal anxieties associated with being sick through play. Doctor, nurse, hospital, or operation games are not infrequently seen in children who have been sick. The child whose premorbid patterns of dealing with difficult situations are constructive utilizes this form of play for only a relatively short time. In some less emotionally sound children prolonged preoccupation with this form of play is a symptom of the persistent unresolved anxieties.

PERSISTENT DEPENDENCY REACTIONS

There is another group of children who, more or less conditioned by the temporary security on an immature level which the illness has brought them, may try to perpetuate the infantile relationships to the environment which have given them a measure of spurious satisfaction. All of us who have had periods of hospitalization or severe illness are personally familiar with the let-down feeling which comes on leaving the hospital or resuming more normal activities. There are a few children who give up the secondary gains of illness most reluctantly even though they presented no particular symptoms of maladjustment prior to the illness. Children who were in an emotionally insecure state before their illness are especially likely to cling to these satisfactions. The attention, fussing, new toys and the like, although not appropriate satisfactions for their emotional needs, do tend to allay some of their anxiousness, no matter what the underlying causes.

The most persistent passive dependent infantile states which emerge out of the focus of a physical illness are those where there is a great deal of intense

anxiety in the parent arising out of the illness of the child. This depends on the role of the child and his illness in the psychic economy of the parent. There may be a great deal of underlying hostility toward the child and guilt-laden feelings about this which bring out markedly unreasonable and irrational fears in the parent. There may be a marked need in the parent of an infantile love object; the fear of loss of the child through the illness intensifies the parent's anxiety and helps the child to maintain his regressive personality functioning brought on by the illness. The parent may have then relatively little impetus to help the child regain his previous level of maturity; the child's passive dependent infantile status fits so well into the parent's own underlying psychological needs. Other parents may feel guilty and anxious about their failure to have prevented the illness in the child, unrealistically believing that they should be able to prevent all illnesses in their children.

Whatever the factors in the parent which determine the degree of neurotic anxiety about the child's illness or which serve as triggers to release the anxiety, the intense emotional state of the parent tends to increase the emotional and social regression in the child and to perpetuate the reaction. To children with such anxious parents hospitalization and its attendant separation from the parent come as destructive, intensely traumatic experiences. The most difficult children to separate from the parents when hospitalization becomes necessary are those whose parents are torn with anxiety and are themselves fearful of being separated from the child. For these children, fortunately a relatively small percentage of those whom we have observed over a period of years, the ordinary ways in which we try to humanize the process of hospital admission and which are successful in allaying or preventing excessive separation anxiety in most children, are of little help. This group of hyperanxious parents and their emotionally disturbed children give considerable concern to hospital administrators, physicians, and nurses. The emotional problems in the child are as a rule of long standing but are made worse by the illness and the new emotional turmoil arising out of the illness in the child; the child is often severely enough upset emotionally that the treatment of his illness is hampered. The presence of the parent may allay some of the more recent intensifications of the emotional disturbance which arise out of the separation and hence aid in the clinical management of the sick child. The presence of an agitated and anxious parent, on the other hand, takes up an unconscionable amount of the time of the hospital personnel; the neurotically irrational nature of their surface concerns makes them unaffected by reassurance and explanation on a realistic basis. The presence of such parents complicates the diagnostic and treatment measures addressed to the child, their presence becomes disturbing to other children on the ward and most often such parents are asked to stay away, in self-defense, by the hospital authorities.

Clinical psychiatric experience with children shows that the exclusion of such parents, no matter how troublesome they are to the hospital staff and may appear to be to the sick child himself, may not be wise. When these children are seen at a later date the psychic trauma of the separation from the parents during the illness is seen as an event which further upsets the pattern of emo-

tional and social growth and development in the child, and which, for the parent, serves as an additional focus for guilt, anxiety, and disturbed feelings which in turn lead to further functional aberrations of the parent-child relationship. In the light of clinical experience the best way of handling such situations would be, if at all possible, to let the parent remain with the child at least during the first day or two of hospitalization. Suitable isolation is necessary to lessen the ill effects of such an arrangement on the other children in the hospital. The unrealistic complaints and concerns of the parent should be handled with an awareness of what the underlying factors might be and an attempt should be made to deal with them on that basis.

It is certain, in the case of the emotionally disturbed child who becomes physically sick, that the period of the illness is a poor time to try to do much about his basic emotional disturbance; it is an equally poor time to add further avoidable stress to his already upset emotional life. During the illness, however, much can be done to help the disturbed parent and thus prepare the way for a more successful convalescence on the part of the child as well as for some direct help with his personality disturbance after he has sufficiently recovered from his illness.

There is a group of what we might term pseudo-anxious parents whose surface behavior is similar to that described above but is not rooted deep in their personalities. They seem to be responding to a particular cultural pattern which expects them to weep, wail, and cling to the child when he becomes ill without real conviction on their own part. They give up this form of reacting quite easily when someone in authority assures them that it is all right to act differently.

REBELLIOUS REACTIONS

Some other children handle the situation of illness and convalescence by developing resentments and rebellion against those who will not let them get back into the swing of things as soon as they would like to. They tend to blame others for the illness and their transient incapacitation. The management of the convalescent period is likely to be most difficult with these children, particularly if it is prolonged. The period of resentment and rebellion may begin almost at the outset of the illness or may start gradually or suddenly after the acute stage has begun to wane. This response in many of the children who exhibit it seems to be related to their anxiety over the theme of illness as a punishment. They often have fears of permanent injury as a result of the disease or operation and their behavior reaction serves to deny, in a compensatory manner, the presence of these fears.

CHRONIC INVALID REACTIONS

The hypochondriacal invalid reaction often follows an episode of physical illness. The illness need not have been a severe or a lengthy one. However, in some of the more drawn-out illnesses the child whose previous tendency is to have feelings of inadequacy and hopelessness, may develop rather alarming hypochondriacal responses which materially interfere with the over-all program

for therapy and convalescence. Parental overconcern is the more important factor in most instances; this continues long after there is any need for a realistic concern about the effects of the illness and contributes directly to the child's continued preoccupation with bodily functioning.

The prolongation of sick-bed practices long after there is any reason is frequently seen. Some parents believe that something still is the matter with the child long after the period of convalescence has begun and at times long after it should have been complete. Other parents remain concerned not that something is the matter but that something might get to be the matter with the child. They are preoccupied with minor fluctuations in the temperature, weight, appetite, color of the skin, consistency of the stool; in fact, no aspect or function of the child is safe from the anxious inspection and concern of the parent. Often a careless word by the child's physician is seized on as justification for the marked concern. Pseudodiagnoses made by interested friends, teachers, nurses, and even at times by some physicians, fan the parental anxieties and lead to further overconcern. Such "diagnoses" are in the nature of "a touch of," "verge of," "if it had gone a little further it might have been," and the various types of "inward" manifestations of almost all diseases. Occasionally physicians thoughtlessly contribute to the development of this picture of chronic invalidism through overtreatment of what are essentially minor and self-limited diseases. At times they are more or less pushed into these unnecessary procedures by the aggressive, demanding attitude of the medically erudite, overanxious parent who presses with questions as to "Aren't you going to do this?" or "Why don't you do this?" The physician who gives in to these pressures has done his patient a disservice and has not helped the parents to approach the problem of illness in their child in a constructive way. It is unfortunately much easier to educate a child into the hypochondriacal invalid reaction than it is to lead him and his parents out of it.

MANAGEMENT OF CONVALESCENCE

The physician's responsibility to the sick child does not end with the cessation of the acute illness. An important part of the total job remains—the supervision of the convalescent period, which continues, except where the disease process leaves handicapping residuals, until the child is able to resume his former activities. During the convalescent period the physical changes caused by disease are repaired and the child returns to the level of maturity present before the illness.

The first step is stopping sick-bed practices when they are no longer necessary. The child is encouraged to participate more actively in his physical care and the number of times per day his temperature is taken is decreased. He is kept out of bed for increasing periods of time and encouraged to associate with other children. This reestablishment of personal relationships through group activities is, with most children, relatively easily accomplished. With the development of interests in the group activities the child gives up the increased personal attention from the nurse or mother, which was necessary while he was acutely ill, much more easily than when he is left to his own resources alone and apart from other children. It is a matter of common observation that chil-

dren on the hospital ward convalesce much more rapidly than do those isolated in separate rooms. Through group activities the child is eased back to reality by a repetition of the processes through which he has already lived in passing from one stage of his social and emotional development to another. There is a slight danger with some children when an over-enthusiastic physician or nurse, recognizing certain immaturities in a child, may try to push him too rapidly to a level of maturity which he had not attained before the illness. Liss believes that the school aged child benefits considerably in his convalescence if he is exposed to some of the learning processes, especially in the arts and crafts, which are more or less normal activities of this age. Through the resumption of normal living experience on a graduated scale the child finds his way back to health. Liss also believes that the knowledge and experience of the educator is of importance in dealing with these aspects of the child's convalescence. The hospital which has the services of a recreational or occupational therapist is most fortunate here even though many such individuals are quite lacking in ingenuity in finding stimulating and satisfying experiences for children of different age groups. There is too often a tendency to fit all children into the same type of activity and not to find out the individual needs and interests of the different children. In our own experience we have found the offices of the public school teacher assigned to the hospital invaluable in promoting convalescence in older children.

If the convalescence is to be carried out in the home the ingenuity of the physician and parent may be severely taxed to provide the opportunities for the child to reestablish his personal relationships through group activities which are in keeping with the state of the child's physical stamina of the moment, as well as to provide the other activities which will bring the child's interests away from his bodily functioning where they had retreated during the illness. If the convalescence is well handled with the full participation of both the parent and the child, there will be relatively few persistent pathologic personality reactions in the child. Attention to the parents' worries and concerns and what is behind them during the period of illness will be helpful in promoting a smooth return to health.

SUMMARY

Emotional disturbances in children often develop in the setting of physical illness. An understanding of the meaning of the illness to the child is helpful in the prevention of lasting emotional upset. To many children illness comes as punishment. A common psychologic reaction is a regression to an immature level of social and emotional adaptation. While many children react to illness in a constructive way, others may respond with persistent dependency patterns, rebellion, or chronic invalid reactions. Attention to the psychologic needs of the child during the convalescent period is also important in the over-all care of the sick child.

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Convalescent Care

STANDARDS FOR CONVALESCENT HOMES FOR CHILDREN

PREPARED BY A SUBCOMMITTEE* OF THE COMMITTEE ON PUBLIC HEALTH RELATIONS OF THE NEW YORK ACADEMY OF MEDICINE

FOREWORD

Standards for convalescent care were first formulated by the Committee on Public Health Relations of The New York Academy of Medicine in 1925. The section relating to the care of children was revised in 1934 to bring it into conformity with evolving pediatric practice. The far-reaching changes of more recent years have again made obsolete some of the earlier recommendations; hence the present restatement of the standards.

I. PURPOSE OF A CONVALESCENT HOME

A convalescent home for children should provide good institutional care in a physical and psychologic environment conducive to enhancement of physical and mental health.

II. NEED OF CONVALESCENT FACILITIES

The benefit which children derive from proper convalescent care is often more marked than is the case with adults. Children are naturally prone to recover from disease. Only a small proportion become long-term patients. With wise psychiatric guidance the emotional involvements of childhood can often be straightened out to prevent chronic invalidism.

The great majority of children in convalescent institutions come from homes where competent physical and psychologic handling is lacking. A convalescent institution, therefore, has the opportunity to provide a well-rounded therapeutic program which will prepare the children for a fuller life in their home surroundings.

This report is limited to the consideration of convalescence in institutions and does not deal with the placement of children in foster homes. The Committee suggests that foster-home care be carefully studied to determine its possibilities for expansion and improvement.

III. GENERALIZED HOMES

The fact that most convalescent homes accept children who are recovering from a wide variety of medical and surgical conditions is proof of the need for the generalized type of home.

IV. SPECIALIZED HOMES

The specialized type of home, with appropriate equipment and personnel, is needed for children requiring special care. In this group are patients suffering from cerebral palsy, orthopedic defects, neurologic conditions and rheumatic fever.

*The Subcommittee consisted of: Samuel Z. Levine, M.D., Chairman, Hugh Chaplin, M.D., Howard R. Craig, M.D., Reginald A. Higgons, M.D., Alfred G. Langmann, M.D., Milton J. E. Senn, M.D., E. H. L. Corwin, Ph.D., Secretary.

V. ADMISSION

A. Policies.—A convalescent home should accept children under 2 years of age only if it has a nursery, and even then preferably for short-term periods. For these young children, foster-home care under competent supervision by responsible authorities is preferable.

Those above the age of 12 years require special personnel and facilities, and they should not be admitted to a children's convalescent home lacking these essentials.

Special dormitories should be available for boys and girls over 10 years of age. Sex segregation should not be maintained during work and play if adequately supervised.

There should be no discrimination on the basis of race, creed, or color.

Children should not be admitted to institutions for adults unless separate accommodations are available. The diet, daily routine, and the type of personnel for a children's home differ from those in a home for adults. Experience has shown that intermingling of the two groups detracts from the benefits to be derived by either.

B. Charges.—Since convalescent homes serve primarily those of the lower income groups, there should be no rigid regulations with regard to charges. The economic situation of each child's family should be investigated by a social worker, and the charge determined on the basis of the report and the probable period of care required. Children are sometimes discharged from convalescent homes before their condition warrants release because the prolonged stay strains the family resources. In such instances, rates should be adjusted.

C. Types of Patients.—For the guidance of administrators, who are frequently perplexed as to the suitability of patients for admission, the Committee has drawn up a list which may be helpful. The list is intended only as a guide.

TYPES OF PATIENTS SUITABLE FOR CARE IN GENERALIZED CONVALESCENT HOMES

I. Post-acute illness:
   - A. Medical
   - B. Surgical

II. Subacute and chronic illness:
   - A. Rheumatic disease:
     1. Chorea
     2. Rheumatic arthritis (low grade)
     3. Cardiacs—functional classification of patients
        - a. Class I (patients with no limitation of physical activity) in any home
        - b. Class II (patients with slight limitation of physical activity) in any home
        - c. Class III (patients with marked limitation of physical activity) in homes with facilities for restricted activity
        - d. Class IV (patients unable to carry on any physical activity without discomfort) in homes with facilities for bed care
   - B. Diseases of long duration requiring special diets and medical supervision:
     1. Diabetes mellitus (in the regulated stage)
     2. Celiac disease (in the regulated stage)
     3. Nephrosis (selected cases)
     4. Colitis
     5. Chronic skin disease requiring nursing care, e.g., eczema

6. Asthma of allergic or infectious origin
   (Patients with wind-borne pollen allergies are not suitable for convalescent homes in rural areas)
7. Congenital syphilis (if long-term care is indicated)
8. Closed tuberculosis (i.e., pleurisy with effusion) if bed care is available
9. Chronic infections, e.g., chronic mastoiditis, osteomyelitis

It is impractical to specify the length of stay of patients suffering from these chronic diseases. If a patient's home is unsuitable for his return, he should remain in the institution as long as the care he receives there is superior to that which he might receive in his own home.

III. Malnutrition
   A. Tuberculin-positive (no open or active lesions)
   B. Tuberculin-negative

IV. Orthopedic disorders
   A. Ambulatory patients who do not require specialized orthopedic treatment acceptable in any home
   B. Bed and ambulatory patients who require special care in homes with special equipment

V. Emotional problems in which a neutral environment plus experience in group living under intelligent supervision might be beneficial

(Psychotic or feebleminded children are obviously not included in this category. Only patients who exhibit symptoms which a competent diagnostician considers to be of basically psychogenic origin should be accepted. Homes which do not have competent psychiatric advice available should not accept children with emotional problems.)

VI. Preventorium care
   Children who have been exposed to active tuberculosis in their homes may be admitted temporarily if they have shown negative reactions to tuberculin tests or positive reactions without active or open lesions. In the latter instance, an x-ray of the chest should be taken before admission.

In general, administrators should give preference to patients recovering from acute illnesses and should accept patients for long-term care only when there is a favorable prognosis.

Attention is directed to the fact that many institutions for convalescents also accept well children for vacation periods in the country, especially during the summer. This practice should be discouraged. Such vacations for well or almost well children are better provided by other agencies. Their exclusion helps to keep the standards of the strictly convalescent home at a high level.

Variations in seasonal occupancy may be obviated by affiliations with one or more hospitals to assure a steady flow of patients.

D. Transportation.—Whenever possible, one or both parents should accompany a child to the institution. If this is impossible, it is recommended that a representative of the institution meet the child and the parent at some convenient point. The opportunity is thus afforded for the parent to give the institution information about the child's behavior and background which may be helpful toward a satisfactory adjustment.

Institutions that admit both children and adults should, when possible, arrange separate times for admission of the two groups. The practice of transporting both groups at the same time may be accompanied by friction.

E. Records.—The Committee wishes to stress that records of the child's illness should *arrive with the child.* Too many children are admitted to convalescent homes with no indication whatever as to the type of treatment, medica-

tion, or diet they have been receiving. Absence of this important information may place the staff at a serious disadvantage if an emergency arises.

The Committee does not desire to specify in detail the form and content of the records of reference, but only to state that they should be as informative as possible in order that the staff may understand the background of the patient. If a convalescent home is associated with a hospital, the hospital record should accompany the child, and should be returned to the hospital, together with the report of convalescence, when the child is discharged from the home.

If an unaffiliated institution receives patients directly from a hospital, a full abstract of the hospital record should accompany the patient, and should remain with the record of convalescence at the home. When a patient is admitted from his own home, the family physician should prepare a comprehensive summary of the child's illness for the information of the convalescent home; this statement should accompany the child. In the last two instances, a report on the child's progress in the home should be forwarded to the referring hospital or physician.

F. Social Service.—Large institutions should employ at least one full-time social worker. A small institution should obtain at least the part-time services of a social worker. Two or more homes in adjacent areas may arrange to share the services of one worker. Small homes in isolated areas may be able to "borrow" social service or visiting nurse service from public agencies.

The social worker at the convalescent home or the visiting nurse acts as a liaison officer between the parents and the institution. Her initial interview with parents of a convalescent child and the hospital social worker should elicit information not only on the economic status of the family, but also on the child's background. Such knowledge may be helpful in preparing the way for proper adjustment in the home. The social worker has other important duties when the child is discharged; these are discussed under Discharge Policies.

G. Examinations.—A physician should examine each new patient within twenty-four hours of admission, if he does not come directly from a hospital. When a patient is admitted directly from a hospital, the examination should be made not later than forty-eight hours following arrival.

It is impractical to isolate patients prior to the admission examination. Few institutions have proper facilities for isolation and, furthermore, certainty of the absence of communicable disease would, in some instances, require isolation for as long as four weeks. Air sterilization affords a more effective and practical method of controlling the spread of communicable disease than the maintenance of facilities for isolation.

VI. MEDICAL SUPERVISION AND CARE

A. Physicians.—During recovery from illness, children should have competent medical supervision. Every convalescent home for children should have on its paid staff a well-trained physician, preferably a pediatrician. A volunteer medical staff sometimes takes its responsibilities too casually. Moreover, it is important for the administrative and medical staffs to work in close cooperation if patients are to receive the best possible care.

Physicians trained in both pediatrics and psychiatry should be available on a consulting basis. In remotely located homes it may be possible to arrange with state mental institutions for the services of psychiatrists as consultants.

B. Medical Examinations.—Medical examinations should be made upon admission and discharge and as often as necessary in the interim. Long-term patients should be examined at least once a month.

C. Nurses.—There should be four graduate nurses to every fifty patient-beds and at least one graduate nurse in residence and on duty at all times, both day and night.

D. Attendants.—A convalescent home for children should provide at least one trained attendant for every ten patient-beds.

E. Dietitian.—An experienced dietitian should be on the staff to supervise the planning and preparation of general and special diets. In small institutions, arrangements should be made for the part-time services of a dietitian.

F. Recreational Therapist.—Every institution, irrespective of size, should have one staff member who supervises the children's recreation. The recreational therapist should be sufficiently well trained to be able to arrange varied activities according to the needs and abilities of the patients, always in close cooperation with the physician.

G. Teachers.—Provision should be made for children of school age whose convalescence is prolonged to continue their schoolwork while they are recovering their health. Teachers may be sent from local or state agencies, or they may be employed by the homes. The child's attendance at classes and the work required of him should be subject to the approval of the physician. Convalescent homes which accept bed patients should make arrangements for bed-ridden children to attend school if their physical condition warrants. The psychologic advantage to a convalescing child of being able to continue his schooling can hardly be overemphasized. His social and psychologic adjustment to normal life may depend upon his ability to rejoin his school class.

H. Ancillary Service.—The amount and type of ancillary service needed depend upon the type of patient admitted to the institution and upon the size of the institution.

As has been suggested earlier, employment of a full-time social worker is recommended for institutions whose size justifies the expense, and social service on some basis should be available to all homes regardless of size.

All convalescent homes should have psychologists and dentists on their staffs, at least on a part-time basis.

I. Kitchen Staff.—There should be cooks, waitresses and kitchen maids, the number to be determined by the size of the institution. In small institutions one person might fill all three positions. The planning of meals should not be left to the cook; presumably she has not had training in dietetics and would not understand the needs of the various types of patients.

J. Maintenance Staff.—The size of the institution will determine the number and type of maintenance personnel. Every institution will require at least one ward maid and one porter. Large institutions may need an engineer, an

electrician, a gardener, a carpenter, and others. Small institutions can probably combine all of these functions in one or two persons.

In planning occupational therapy for the children it may be possible to employ members of the maintenance staff as teachers if they have been carefully selected. Any time lost by a worker in using the children as "helpers" may be well worth while if it enhances the children's morale by making them feel useful. Such work therapy should be carried out only with the full knowledge of the physician and under his direction as to the amount and type of "help" which may be given by the patient.

K. Volunteers.—Admittedly the standards here formulated may not be attained without extensive changes in present practices. The element of cost has not been discussed because wide variations in local conditions preclude any general statement of this item. It is recognized, however, that expense may be a deterrent to the realization of many of the recommendations here set forth. It is suggested that community support for the work of convalescent homes should be enlisted in every way possible. Such support might be expressed not only through financial contributions to the institution, but through an active program for recruitment of volunteers who may give valuable service under the supervision of the trained staff. Volunteer help may be used at various levels of service, such as nursing, recreation, social work, transportation, and general housekeeping.

VII. REGIMEN

The details of the daily program should naturally vary with the physical condition of the children. Those needing but a short convalescence could probably be more active than those requiring a longer period to regain their health. A routine of sufficient variety to hold interest should be mapped out for each child.

The regimen should be properly balanced as to rest, play, exercise, and therapy, with some free time each day for elective activity within the limitations of the child's physical condition. A rest period of from one to two hours should form part of the daily routine. Rest periods will require supervision as much as will the play, work, and exercise periods, but care should be taken to avoid rigidity and militarism in the supervision of any activity.

VIII. DIET

A high level of nutrition should be maintained by providing sufficient wholesome, nourishing food, properly cooked and attractively served. The best balanced meal in the world is of no value if it is left on the plate because of improper preparation. It is particularly important that food should be of the proper temperature. In institutions for children, small "treats" in the diet may serve a useful psychologic purpose.

The matter of eating between meals should be left to the discretion of the physician. Extra nourishment may be essential for some children, perhaps in small meals at frequent intervals.

It goes without saying that the physician is the arbiter who prescribes special diets, and the dietitian should be sufficiently trained to plan and arrange them.

IX. TEACHING POSSIBILITIES

Many institutions do not make use of the excellent opportunity they have to inculcate health habits in the children and to teach them rules of hygiene and health. Stressing the importance of fresh air, sunshine, rest, and a proper diet in their everyday routine is a practical way of teaching them how to live and how to keep well.

It is the duty of every convalescent home to train the children under its care to a daily routine, thus starting good habits which may continue after discharge. The children should become accustomed to regular lives and to the practice of good health habits.

In addition to the valuable work which a convalescent home can do in teaching children proper habits of health and hygiene, it can also render an important service in the training of student nurses and interns. The presence of such personnel would be valuable to the home, and the opportunity to observe convalescent patients would be advantageous to the students.

X. RECORDS

Few institutions keep proper records of the children in their care. Some make no attempt to keep any medical or health record other than the diagnosis on the admitting slip and a notation of the child's weight; in many instances, the weight records are kept in a separate book. A carefully kept history of a patient's progress in a convalescent home would be of great value in the event of a later illness. Good records are also of incalculable value for research.

Assuming that a comprehensive history of the child's illness and treatment is presented at the time he is admitted to the institution, the convalescent home should add to it all the important facts of the child's progress during his stay in the home, including his psychologic as well as his physical adjustment. A detailed history should be kept of any illness which occurs while the patient is in the convalescent home.

XI. VISITING

Rules regarding visits to patients should not be rigid. The size of the convalescent home, the type of patients admitted, and the age of the patients will undoubtedly be determining factors in the formulation of the rules.

Since the welfare of the patients should be the first concern of the convalescent home, the psychologic value of frequent visits by the patient's family should be carefully weighed against the possible danger of contagion.

XII. DISCHARGE POLICIES

The discharge of a patient should be authorized by the physician in charge. This decision should not rest with the superintendent, as it does in many institutions at the present time.

As has been stated in a previous section, a patient should not be discharged because of inability to pay; the financial status of the family should be studied and a rate of payment agreed upon which makes possible the optimum stay in the home.

The aim of convalescent homes should be the attainment of optimum care and improvement in the health of children, and this aim should not be sacrificed by the admission of too many patients in relation to facilities and personnel.

Whenever possible, the institution's social worker or a public health nurse should visit the patient's own home prior to his discharge to determine whether discharge to that home is advisable. Investigation may reveal an acute illness or some other remediable condition which a relatively short additional stay in the institution would enable the child to avoid.

It is desirable for parents to take a child from the institution, but when this is impossible, the transfer should be made by the social worker or by a public health nurse.

When a long-term patient is discharged, the institution should furnish to the authorities of his school a report of the child's progress in his schoolwork while in the home. Such a report will assist the authorities in placing the child in the proper group when he returns.

XIII. FOLLOW-UP PROCEDURES

The social worker or a public health nurse should visit the patient's home when he is discharged and should make an additional visit from three to six months later in order to evaluate the patient's progress and the benefit derived from his stay in the institution. A report of this follow-up visit should be filed with the complete record of the case. The interval between the discharge and the date of the follow-up visit would be determined by the type of illness for which the patient was admitted to the institution.

XIV. PLANT

Some maintain that convalescent institutions for children should be located in rural and semirural areas in order to supply a maximum of fresh air, sunshine and freedom of movement. Others are of the opinion that such institutions should be located in urban areas, where they may have the advantage of readily available hospital staffs and facilities. Suburban communities would meet the need for fresh air, sunshine and freedom of movement, and at the same time the distance from hospitals would not be so great as to discourage visits by consulting physicians, and the transportation to hospitals for special treatment could be arranged without too great difficulty.

The optimal capacity of a convalescent home for children is from fifty to seventy-five beds. The Hospital Facilities Section of the United States Public Health Service has worked out plans which afford assistance to those concerned with the construction of convalescent institutions. The proportion of beds to be allotted to patients requiring long-term care is a matter of policy on the part of each institution.

XV. RESEARCH

The basic facts of convalescence are not well established. There is a well-recognized need for research on the clinical and biochemical, as well as the organizational and social aspects of convalescence. It should, however, be emphasized that adequate research cannot be undertaken without proper facilities,

personnel, record-keeping, and funds. Since few convalescent homes for children possess all these advantages, research programs should be instituted only in homes having the proper staff and facilities to conduct well-thought-out programs.

XVI. GRADING AND LICENSING

Nowhere in the country is there adequate supervision over convalescent homes. A number of states now have laws requiring that hospitals and related institutions be licensed, but the requirements vary from state to state. In some states the licensing is done by the departments of welfare; in others, by departments of public institutions or departments of health. Official inspections of convalescent homes are, as a rule, limited to the physical plant; little or no attempt is made to gauge the quality of care rendered. Every state should include convalescent homes among the institutions for which licensing is required and should provide for adequate qualitative inspections of these homes.

Comments on Current Literature

Q FEVER

TWO naturally occurring outbreaks of Q fever have been reported in the United States, the first in Amarillo, Texas, in March, 1946, and the second in Chicago, Ill., in August, 1946. Both sharp outbreaks occurred among slaughter-house workers who had come in contact with tissues and body fluids of infected cattle or sheep. An arthropod vector did not seem to be involved in these American outbreaks, as apparently had been the case in other outbreaks. Infection of human beings presumably occurred by direct contact or by means of droplets of splattered fluids. However, in these two explosive and isolated outbreaks, the manner in which the animals had become infected was not determined, nor was it possible to gain a clear idea of the natural reservoirs of Q fever in the United States.

The occurrence of Q fever in an apparently endemic area in California offered opportunity for further study of this rickettsial disease. In the June issue of the *American Journal of Public Health,* Shepard and Huebner[1] report studies concerned with the occurrence of Q fever in Los Angeles County in the so-called milk shed area situated ten to thirty miles southeast of the center of the city. In this endemic area, the diagnosis of Q fever was based on typical clinical history and on confirmatory laboratory findings. In their report, Shepard and Huebner[1] give as the typical clinical history the following:

"The onset was acute with fever, headache, chills or chilly sensations, and body aches and pains. Cough was frequently complained of but was not a prominent symptom. The sputum which was sometimes produced was at times blood-tinged. Chest pain was common and was usually of a lateral distribution, although a feeling of substernal congestion was frequent. Physical examination of the chest often revealed little of note except perhaps suggestive findings. Respirations were elevated when pneumonic involvement was extensive. Roentgenography revealed a pneumonic process which was usually diagnosed as "atypical" pneumonia when patchy, and "early lobar" pneumonia when diffuse. The leucocyte count tended to be normal or slightly elevated. The illness ran a course of one to three weeks' fever with prolonged convalescence especially in older patients. No deaths were found which could be attributed to Q fever."

Confirmatory laboratory diagnosis includes demonstration by complement-fixation serum tests of type-specific antibody, especially increasing titer during clinical recovery, and isolation of the etiologic agent, *Richettsia burneti,* from the blood during acute illness.

Seventeen human cases of Q fever were diagnosed in the Los Angeles area. Although none of the clinical cases occurred in dairy workers, all but two patients gave a history of having visited dairies or of having lived near them. On the other hand, one-half of the dairy workers tested were shown to have positive complement fixation tests for *R. burneti.* The lack of clinical manifestations or of history of illness in these subjects suggested that many had undergone mild or inapparent attacks of Q fever.

From an epidemiological viewpoint it is significant that sixty sera of beef cattle from Texas and adjacent states and more than sixty sera from Maryland milk cows were found negative for complement fixing antibodies for Q fever, whereas of 130 bovine sera from the Los Angeles area, 21, or 16.2 per cent were

found positive. However suggestive, these results do not make it possible for the authors "to state definitely that the cows are the source of human Q fever infection, since the possibility remains that the same source infected both cows and man."[1]

In this connection, a paper by Huebner, Jellison, Beck, Parker, and Shepard,[2] reporting the isolation of *R. burneti*, the causative agent of Q fever, in samples of raw milk from four dairies in southern California, suggests another possible mode of transmission. Pasteurization, even under field conditions, apparently rendered naturally infected milk noninfectious for guinea pigs. However, these authors state that available epidemiological evidence does not indicate that the drinking of milk was the cause of a majority of the cases thus far studied.

In searching for specific therapy of Q fever, Huebner and Hottle note that streptomycin has been found to exercise rickettsiostatic action on the causative organisms of epidemic typhus, endemic typhus, Rocky mountain spotted fever, and rickettsialpox. In the March 19th issue of the *Public Health Report*, Huebner and Hottle[3] report that streptomycin exerts a rickettsiostatic action on *R. burneti* in experimental infection of embryonated eggs and guinea pigs. Of particular interest were their results with guinea pigs. Although the number of animals used was small, it was shown that nineteen of twenty-four guinea pigs receiving subcutaneously 40 to 50 mg./kg. of body weight of streptomycin three or four hours after a large inoculation of *R. burneti* survived, whereas twenty-seven of the twenty-eight controls not receiving streptomycin died.

The complete reporting of Q fever must depend upon increased awareness of its presence by physicians and the adequate use of laboratory diagnostic facilities. Further studies of Q fever promise to clarify the natural history of the disease and will afford opportunities for possible control. As more work is done with rickettsiostatic and rickettsiocidal agents, particularly the newer antibiotics, adequate therapy of rickettsial diseases, including Q fever, will be forthcoming.

RUSSELL J. BLATTNER.

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News and Notes

The Transactions of the **Fifth International Pediatric Congress,** held in New York, July, 1947 will appear in Vol. XXXVI of *Acta Paediatrica.* Price 25 Swedish crowns. Orders should be sent to the following address: Acta Paediatrica, Polhemsgatan 30, Stockholm, Sweden.

General Index to Vols. I-XXX of *Acta Paediatrica* has been published and may be obtained for 15 Swedish crowns.

The pediatricians in the Union of South Africa have formed the **South African Paediatric Association.** It is formed within the Medical Association of South Africa and has been recognized by the Federal Council of that association. The Chairman is Dr. Basil Melle, and the Secretary-Treasurer, Dr. Seymour Heymann.

The Kaiser medal for outstanding medical service was awarded to Dr. John Aikman, assistant professor of pediatrics at the University of Rochester School of Medicine, by the Rochester Academy of Medicine on May 4.

At the annual meeting of the **American Pediatric Society,** held in Quebec in May, the following officers were elected:

President: Jean V. Cooke, St. Louis
Vice-President: Lawson Wilkins, Baltimore
Secretary-Treasurer: Henry G. Poncher, Chicago

The **Second International Symposium on Feelings and Emotions** is being sponsored by the Loyal Order of Moose, with the cooperation of the University of Chicago, on October 28, 29, and 30. Dr. Martin L. Reymert, Director of the Mooseheart Laboratory for Child Research, is General Chairman, and Dr. Anton J. Carlson, professor emeritus of physiology at the University of Chicago, is Honorary Chairman. From forty to fifty scientists will contribute to the discussion at Mooseheart, Ill., among whom will be:

John E. Anderson, The University of Minnesota
Chester Darrow, Illinois Institute for Juvenile Research
John Elmgren, University of Gothenburg, Sweden
Arnold Gesell, Yale University
Harold Jones, University of California
James G. Miller, University of Chicago

Detailed information can be obtained by writing Dr. Reymert at Mooseheart, Ill.

The Department of Pediatrics, Washington University Medical School, announces a two-month refresher course, September through November. The entire field of pediatrics will be covered. The course will be given at the St. Louis Children's Hospital, fee $200. Detailed information may be obtained from the Director of Post-Graduate Studies, Washington University School of Medicine, 4580 Scott Avenue, St. Louis 10, Mo.

The American Academy of Pediatrics' **Committee for the Improvement of Child Health** will take over their new office at The Children's Hospital of Philadelphia, 18th and Bainbridge Streets, on July 1. Dr. John P. Hubbard is Director of this Committee. In addition to his work with the American Academy of Pediatrics, Dr. Hubbard will conduct a rheumatic fever teaching program throughout Pennsylvania under the auspices of the State Health Department.

Book Reviews

Psychopathology and Education of the Brain-Injured Child. Alfred A. Strauss and Laura E. Lehtinen, New York, 1947, Grune & Stratton, pp. 206. Price $5.00.

This book is certainly required reading for anyone who undertakes the education of children with cerebral palsy or other cerebral difficulties. The discussion is properly concerned with the psychologic factors which modify educational plans. The handling of this part of the problem is skillful and authoritative. The selection of appropriate tests is discussed, and the authors point out the dangers of relying on tests which are adapted to unhandicapped children.

The medical discussion is, this reviewer believes, less adequate than other parts of the volume, but certainly one major point is important and relevant. The concept that deviations from normal development should be recognized is obviously correct. Pneumoencephalography and electroencephalography are hardly discussed at all, and pathology is discussed casually and without much curiosity. The orthopedic implications are also treated briefly.

After all, the authors were interested in the methods by which children could be educated, in the face of irregularities of mental function. The discussion of this major problem is full, reliable, and helpful. Certainly no other publication gives any such information The great virtue of the book is that it reports the viewpoint of experienced psychologists and teachers in a field which has not been adequately explored by medical men.

B. C.

Infant Nutrition. P. C. Jeans and W. McKim Marriot, ed. 4, St. Louis, 1947, The C. V. Mosby Co., 516 pages. Price $6.50.

A new edition of what has become since its publication in 1930 one of the standard medical texts for students and practitioners. In this edition the name of Dr. Jeans, who prepared the third edition in 1941, rightly becomes the senior name to the text.

The fourth edition has been completely revised and many parts rewritten in keeping with the developments in nutrition which have taken place in the last seven years. Some of the illustrations, such as those showing techniques, are new and in keeping with recent advances. All in all, it is a most satisfactory text and will undoubtedly continue to hold the place it has made for itself in the past.

Year Book of Pathology and Clinical Pathology. Howard T. Karsner, M.D., and Arthur H. Sanford, M.D., Editors, Chicago, 1948, Year Book Publishers, 558 pages. Price $3.75.

This is the first Year Book on pathology to appear since 1941. Dr. Karsner and Dr. Lund, his associate at the Institute of Pathology of Western Reserve University, have selected their material from the most recent literature of pathology rather than attempting to cover the interval since the last edition. Over 200 pages of the text are on Clinical Pathology, edited by Dr. Sanford of the Mayo Foundation, who has followed the same principle. All of the most recent advances in methods are included.

The Baby's First Two Years. Richard M. Smith, M.D., Boston, 1948, Houghton-Mifflin Company, 181 pages. Price $2.75.

A revised, and in many parts rewritten, text of one of the pioneer books on infant care for mothers. The material reflects the many years of Dr. Smith's experience in prac-

tice in that it presents what the average mother wants and needs to know about her baby. The author has kept pace with modern trends and developments in infant care and it is a safe and sane text for parents. Out of curiosity the reviewer compared it with one of the earlier editions of nearly twenty-five years ago (it was first published in 1915), and the changes it revealed which have taken place in pediatrics in the last quarter century are most interesting.

Nursing of Children. Gladys Sellew, R.N., Ph.D., in collaboration with Sisters Annette Walter, M.A., and Ann Harvey, M.A., ed. 6, Philadelphia, 1948, W. B. Saunders Co., 486 pages.

The fact that this is the sixth edition of Sellew's text on pediatric nursing since it was first published in 1926 is evidence that it has found a definite place in nursing education. The book contains a little bit of everything about children and the care of children. In fact, the chief criticism is that it is too expansive and the important is mingled with the unimportant. It contains far more than the average student nurse needs to know or should be expected to know. The text strolls far from the subject of the nursing of children. A careful and judicious pruning of the book, to about two-thirds of its present size, would make it much more useful.

Editor's Column

AN EDITORIAL PROBLEM

ONE of the more difficult problems that comes to the editorial board of a medical journal is the question of papers which either contain new ideas, or report work in which the conclusions are quite at variance with currently accepted viewpoints or practices. This is particularly true when the point of the paper has to do with therapeutic procedures.

Some contend that the publication of such papers puts the stamp of approval of the Editorial Board on the conclusions and findings. If this view were to prevail it would result in nearly every new idea being buried. The other viewpoint is that the work will stand or fall on its merits; if the conclusions are substantiated by subsequent studies by independent workers, much has been accomplished; if for some reason the work is not substantiated, no real harm has been done. An editorial board is not a scientific research group with the function of testing out new ideas before they are published, but it does have a definite responsibility in accepting papers of this nature for publication. There are certain criteria which a board must use. First of all, the conclusions must be logical deductions from the work upon which they are based. A matter of further importance is the recognized scientific integrity of the author or the clinic where the studies were made. We could cite numerous illustrations from medical history where papers have been rejected because they presented ideas contrary to accepted current practice, and later these new ideas or conclusions have proved to be correct. On the other hand, many illustrations come to mind where the ideas or conclusions drawn have turned out to be erroneous.

This discussion has been brought about by the recent acceptance and publication of a number of articles in THE JOURNAL OF PEDIATRICS which fall into this category; for example, the work on the feeding of infants with diarrhea in last month's issue from Dr. Holt's clinic in New York. Most certainly this procedure needs a thorough check by other clinics and investigators before its value can be established or the practitioner can change from the initial starvation period which is the accepted practice of many years. We are sure no one will question the propriety of the publication of the studies by Dr. Holt and his associates, nor would anyone consider the publication to imply that the members of the Editorial Board of the JOURNAL were urging a complete volte-face in the handling of infants with diarrhea. This paper will recall to the older pediatricians the furor that was caused a number of years ago by Coleman and DuBois, who fed their patients with typhoid fever, in contrast to the starvation diet which had been the accepted method of treatment for several

decades. Also in July issue of the JOURNAL, Dr. Adams, a younger and less well-known pediatrician, presented the results of a rather startling simplification of the feeding of premature infants which he experimented with largely by necessity during the war. Again the Editorial Board feels independent confirmation is necessary before the practitioner should turn from accepted methods to these simpler methods.

These are two examples of a number of papers with new ideas and procedures contrary to accepted practice which the Editorial Board of the JOURNAL has accepted for publication. It does not mean that the Editorial Board officially sponsors or advocates the new procedures. The board has, however, the responsibility of presenting new ideas and procedures in the interest of medical progress, even though ultimately the conclusions or work of the authors are found to be faulty. The JOURNAL has rejected papers presenting new ideas when it was felt the conclusions were not warranted by the work upon which they were based, and a few were rejected when, in the opinion of the board members, the proposed procedures carried an element of danger. The Editorial Board of the JOURNAL feels that its readers have the intelligence and judgment to form their own opinions, and that they not only appreciate but desire the stimulation of new ideas which reflect the intellectual curiosity upon which scientific progress depends.